FOREWORD INTRODUCTION

2-NAPHTHOL

CAS N°: 135-19-3

SIDS Initial Assessment Report

For

SIAM 15

Boston, USA, 22-25 October 2002

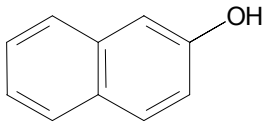
1. Chemical Name:	2-Naphthol
2. CAS Number:	135-19-3
3. Sponsor Country:	Germany / Japan Contact Point: BMU (Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit) Contact person: Prof. Dr. Ulrich Schlottmann Postfach 12 06 29 D- 53048 Bonn
4. Shared Partnership with:	-
5. Roles/Responsibilities of the Partners:	-
• Name of industry sponsor /consortium	In the first stage of the process Clariant was sponsor company. As production has stopped at this company, the industry sponsor has not taken an active role in the further assessment process
• Process used	The environmental assessment was performed by the Federal Environmental Agency (UBA); the human health assessment was performed by BUA (Advisory Committee on Existing Chemicals) and reviewed by the Federal Institute for Risk Assessment (BfR). After that the Japanese co-sponsor reviewed and completed the assessment.
6. Sponsorship History	
• How was the chemical or category brought into the OECD HPV Chemicals Programme?	The substance was selected in phase 3 of the OECD-SIDS program by Germany. Japan has performed the reproductive toxicity study and became so a co-sponsor for this substance
7. Review Process Prior to the SIAM:	SIDS testing plan was discussed at the 3rd SIDS Review Meeting (September 1993). There, it was agreed that a test on reproductive toxicity should be performed
8. Quality check process:	As basis for the SIDS-Dossier the non-confidential IUCLID from the European Chemicals Bureau was used. All information that could not be reproduced was deleted (mainly chapter 1). If this information was used in the assessment, reference to the ECB-IUCLID is made. All other data have been checked and validated by UBA and BUA

9. Date of Submission: 08. August 2002

10. Date of last Update: -

11. Comments: -

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	135-19-3
Chemical Name	2-Naphthol
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

2-Naphthol can be absorbed through the skin. Rapid conjugation with glucuronide and sulphate in the liver and renal excretion of the unchanged and conjugated forms seems to be the principal mechanism of elimination. The acute oral LD_{50} in rats was determined as 1320 mg/kg bw in a study following OECD TG 401. Clinical signs included reduced activity, accelerated breathing, closure of eyes, nasal discharge and diarrhoea, and at exposure levels near to or exceeding the LD_{50} also tumbling, reduced reflexes and seizures.

The inhalation 4-hour-LC_{50} in rats was determined as 2200 mg/m^3 (aerosol; OECD TG 403). Clinical signs included irregular breathing, reduced activity, impaired motility and reflexes, nasal discharge, corneal opacity and diarrhea.

2-Naphthol was not irritating to the skin of rabbits in a test performed according to OECD TG 404, but caused serious damage to the eyes of rabbits in a study in accordance with OECD TG 405 (corneal vascularization/opacity). 2-Naphthol is a skin sensitiser, based on results from a guinea pig maximization test [OECD TG 406]. An increased incidence of contact dermatitis in exposed workers is reported in an old and poorly documented study.

After repeated administration to rats by the oral route for 28 days, there were indications of a possible effect on the adrenals in both sexes at dose levels of 50 mg/kg bw/day and above (increased relative and absolute adrenal weights). At 150 mg/kg bw/day, an increase in serum creatinine and changes in serum electrolytes were found in males, indicating an effect on the kidneys.

Poorly documented studies in dogs and rats involving repeated administration by the subcutaneous and inhalation route showed effects on the liver and kidneys. Concentration dependent disturbances in blood clotting and functional impairment of the liver and kidney with accompanying histopathological effects occurred at 10.1 and 1.35 mg/m^3.

2-Naphthol was not mutagenic in several Ames tests both in the absence and in the presence of metabolic activation, even at cytotoxic concentrations. Inconsistent results have been observed in bacterial DNA repair tests, but it did not induce unscheduled DNA synthesis in rat hepatocytes in a test performed according to current standards. 2-Naphthol was not tested for its potential to induce chromosomal aberrations *in vitro*. In an *in vivo* micronucleus assay with 2-naphthol, no evidence of genotoxicity was found. These data show that 2-naphthol is not mutagenic *in vivo*.

There are no adequate data available for the evaluation of the carcinogenic potential of 2-naphthol.

2-Naphthol was tested for its reproductive toxicity in a one-generation study according to OECD TG 415. The administration of the test substance had no adverse effect on the reproductive abilities of the parental generation. No teratogenic effects were observed (NOEL for male reproductive toxicity: 160 mg/kg bw/day (highest tested dose); NOELs for female reproductive toxicity and for toxicity to the offspring: 40 mg/kg bw/day each). (160 mg/kg bw/day may suppress nursing; reduced body weights and reduced viability was seen in the offspring at 160 mg/kg bw/day). The LOEL for systemic toxicity in males was 10 mg/kg bw/day (salivation), the NOEL for systemic toxicity in females was 10 mg/kg bw/day (nasal discharge, reduced food consumption, decreased

locomotor activity and salivation at 40 mg/kg bw/day).

In workers exposed to 2-naphthol an increased incidence of dermatitis, conjunctivitis, and rhinitis have been reported in poorly documented studies. In addition, changes in kidney function, and an increased incidence in chronic hepatitis and impairment of the nervous system were reported from workers who were also exposed to a variety of other chemicals.

Environment

2-Naphthol has a water solubility of 0.6 - 0.8 g/l, a vapor pressure of 1.4 Pa and a measured log Kow in the range of 2.01 – 2.84. 2-Naphthol is readily biodegradable as shown in a MITI test according to OECD 301C with non-adapted inoculum. A biodegradation of 68 % after 14 days was found. There is no information on the degradation kinetic. The measured log Kow in the range of 2.01 to 2.84 does not indicate a significant potential for bio- or geoaccumulation. With a fugacity model (Mackay I) the following distribution can be predicted: hydrosphere: 83 %, atmosphere: 8 %, soil: 4.5 % and sediment: 4.5 %. The hydrosphere is therefore the target compartment for this substance. In water solution, photodegradation has been observed, but the half-life under environmental conditions was not estimated. The calculated half-life due to photochemical-oxidative degradation in the atmosphere by OH-radicals is about 2 hours.

For 2-naphthol there are short-term tests with fish, invertebrates and algae available. The lowest effects values from the short-term tests are:

Pimephales promelas: 96h-LC_{50} = 3.46 mg/l,
Gammarus minus: 48h-EC_{50} = 0.85 mg/l, and
Nitzschia palea: 4h- EC_{50} = 6.3 mg/l.

As there is no standard algae study available, the ECOSAR model was employed to predict the toxicity of 2-naphthol to green algae, resulting in a 96h-EC_{50} of 12.9 mg/l. This supports that algae are not likely to be the most sensitive species in short-term tests. With an assessment factor of 1000 a PNECaqua of 0.85 µg/l was derived from the 48h-EC_{50} for the most sensitive species, *Gammarus minus*.

Exposure

The worldwide production capacity of 2-naphthol is approximately 100,000 metric tonnes per year. The substance is used as an intermediate for the production of dye-stuffs, pharmaceuticals, fungicides, insecticides and odor agents. The substance is also used as an antioxidant for rubber and plastic, grease and lubricants.

Releases into the environment may occur during production and processing of 2-naphthol and from its direct use as e.g. antioxidant. Further sources are:

- the waste water from the conversion of coal to liquid and gaseous fuel products. A "typical concentration" of 50 mg/l is cited.
- the waste water of the petroleum industry.
- the groundwater near waste sites from wood-treatment processes.

An exposure of the terrestrial compartment is to be expected, as 2-naphthol is a metabolite of the herbicide naproanilide. As no further exposure data are available, the relevance of the exposure of the terrestrial compartment cannot be assessed.

2-Naphthol is a product from the atmospheric reaction of naphthalene (CAS No. 91-20-3) with hydroxyl radicals.

Occupational exposure may occur during production and processing of 2-naphthol. In Germany, the production was stopped in 1992; no workplace exposure information is available with regard to processing sites. From a European production plant workplace peak exposures between 0.0005 and 1.632 mg/m^3 are reported.

Consumers may be exposed to 2-naphthol through cigarette smoke. The use of 2-naphthol in cosmetics is not allowed in the European Union and marketing of medicines containing 2-naphthol is prohibited in Germany.

RECOMMENDATION

Human Health: The chemical is currently of low priority for further work.

Environment: The chemical is a candidate for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: The chemical is currently of low priority for further work based on its low hazard potential. It is noted that the chemical can cause serious eye damage and is a skin sensitiser.

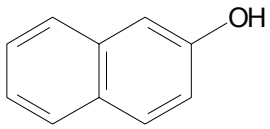
Environment: Little information is available about releases into the environment from production and processing sites and from the direct use of the substance. However, this information indicates that significant releases into the environment may occur. In addition, the relevance of releases into the terrestrial compartment from the metabolisation of the herbicide naproanilide should be clarified. Therefore, an exposure assessment is recommended. This recommendation is based on the high toxicity of 2-naphthol to aquatic organisms. A PNECaqua of 0.85 µg/l was derived from the available short-term data. Dependent on the exposure situation further tests with aquatic and/or terrestrial organisms may be required.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 135-19-3
IUPAC Name: 2-naphthol
Molecular Formula: $C_{10}H_8O$
Structural Formula:



Molecular Weight: 144.17
Synonyms: β-hydroxynaphthalene
β-naphthyl alcohol
Azogen Developer A
C.I. Azoic Coupling Component 1
C.I. Developer 5
Developer AMS
Developer BN
Isonaphthol

1.2 Purity/Impurities/Additives

Degree of purity: ≥ 99 % w/w.

1.3 Physico-Chemical properties

Table 1 Summary of physico-chemical properties

Property	Value	Comment
Physical state	Solid	
Melting point	121 °C	
Vapour pressure	1.4 Pa (20 °C)	extrapolated from measured values of a temperature range of 145 - 300 °C
Water solubility	0.6 - 0.8 g/l (25 °C)	
Partition coefficient n-octanol/water (log value)	log $K_{ow}$is in the range of 2.0101 (HPLC) to 2.84 (shake flask).	
Henry's law constant	0.25 - 0.33 $Pa \cdot m^3 \cdot mol^{-1}$	

1.4 Category Justification

Not applicable.

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

In the EU the production and import volume is in the range of 50,000 to 100,000 t/a (ECB, 2000). The worldwide production volume of 2-naphthol is reported to 60,000 t/a (Clariant, 2001) while the worldwide production capacity is given with 100,000 t/a (China pharmaceutical chemical network). Production sites are located in China, India, Japan, Italy and some east European countries (China Pharmaceutical Chemical Network). The only German manufacturer has stopped its production in March 1992.

2-Naphthol is produced by sulfonation of naphthalene to 2-naphthalene sulfonic acid, and reaction with caustic soda solution to obtain the sodium salt. Reaction of the sodium salt with sodium hydroxide and treating the melt with sulfuric acid yields 2-naphthol.

2-Naphthol is mainly used as intermediate for the production of dyestuffs. Further products are pharmaceuticals, fungicides, insecticides and odor agents. It is not quite clear whether 2-naphthol in these applications serves also as an intermediate or may directly be contained in these products. It is assumed that the main part is used as intermediate. The substance is also used as an antioxidant for rubber and plastic, grease and lubricants (ECB, 2000).

The direct use of 2-naphthol as developing dye seems to be only of historical interest (Ullmann, 1991).

2-Naphthol is not listed in the Danish product register (June 2002). In the Swedish product register (June 2002) and in the Norwegian product register (2001) only confidential data are available. In the Swiss product register (May 2002) there are 3 commercial products that contain 2-naphthol. One product (paint, lacquers, varnishes) contains 2-naphthol in amount of 1 – 10 %, one product (solvent, degreaser) has a 2-naphtol content of 0.1 – 1 % and in a third product (cosmetic) 2-naphthol is contained in amount up to 0.1 %.

2.2 Environmental Exposure and Fate

2.2.1 Sources of Environmental Exposure

Releases into the environment may occur during production and processing of 2-naphthol and from its direct use as e.g. antioxidant. During the processing of 2-naphthol to 3-hydroxy-2-naphthoic acid (BONS) by one German chemical plant, 60 t/a were emitted into the waste water and 116 kg/a into the air. As the processing of BONS has stopped, this source of exposure does not longer exist. From an Italian production and processing site there is the information that 400 t/a are released into the wastewater treatment plant. Various analytical determinations of the effluents have resulted in values below the limit of detection. However, the detection limit is not given (ECB, 2000). At the same site 1.7 t/a are released into the atmosphere. There are no emission data from other sites and uses available.

Further sources of exposure are:

- the waste water from the conversion of coal to liquid and gaseous fuel products. A "typical concentration" of 50 mg/l is cited (Blum et al., 1986)).
- the waste water of the petroleum industry (Liu et al., 1987).

- the groundwater near hazardous waste sites from wood-treatment processes (Rostad et al., 1984).
- 2-Naphthol has been found as a photodegradation product from the herbicide naproanilide used in rice fields (Oyamada/Kuwatsuka, 1986).

2-Naphthol is a product from the atmospheric reaction of naphthalene (CAS-No. 91-20-3) with hydroxyl radicals.

2.2.2 Photodegradation

In water solution, photodegradation has been observed, but the half-life under environmental conditions was not estimated (Oyamada/Kuwatsuka, 1986). The calculated half-life due to photochemical-oxidative degradation in the atmosphere by OH-radicals is about 2 hours.

2.2.3 Stability in Water

In water solution, photodegradation has been observed, but the half-life under environmental conditions was not estimated (Oyamada/Kuwatsuka, 1986).

2.2.4 Transport between Environmental Compartments

Based on the physico-chemical properties, a Mackay I calculation (version 2.1) predicts the following distribution: hydrosphere 83 %, atmosphere 8 %, soil 4.5 % and sediment 4.5 %.

2.2.5 Biodegradation

2-Naphthol is readily biodegradable as shown in a MITI test according to OECD 301C with non-adapted inoculum. A biodegradation of 68 % after 14 days was found (CITI, 1992). There is no information on the degradation kinetic. In an OECD-confirmatory test system, an elimination of 99.83 % (adaptation time 100 d, residence time 48 h) was determined (Bosch et al., 1978). Because of the long residence time it cannot be assumed that the same degradation rate will occur in adapted wwpts. According to the model SIMPLETREAT (EU TGD), in a removal rate of 88 % is predicted for waste water treatment plants (input values: k= 1 h^{-1} (readily biodegradable), log Kow: 2.84, Henry: 0.25 - 0.33).

A biodegradation test under methanogenic conditions (inoculum: primary digested sludge) resulted in 0 % degradation after 75 d (Battersby/Wilson, 1989).

2.2.6 Bioaccumulation

The measured log Kow values in the range of 2.01 to 2.84 indicate that there is no significant potential for bio- or geoaccumulation.

2.2.7 Other Information on Environmental Fate

No data available.

2.3 Human Exposure

2.3.1 Occupational Exposure

Occupational exposure may occur during production and processing of 2-naphthol. In Germany, the production of 2-naphthol was stopped in 1992. No exposure information is available with regard to processing sites.

Workplace measurements are available from an European production plant from the years between 1988 and 1993 (4 departments with 2-18 unspecified workplaces, between 9 and 64 samples per workplace were analysed for 2-naphthol by HPLC; mean values: 0.0005 – 0.078 mg/m^3, max. values: 0.0005 - 1.632 mg/m^3) (ECB, 2000).

2.3.2 Consumer Exposure

Consumers may be exposed to 2-naphthol through cigarette smoke (Commins RT and Lindsey, 1956). Traces of 2-naphthol were detected in bottled mineral water (0.2 - 2.9 µg/l); the source of this contamination was identified as the red colored plastic caps (Manninger, 2001). In the European Union, 2-naphthol is listed as a substance which must not form part of the composition of cosmetic products (EC, 1999). The marketing of medicines containing 2-naphthol, e.g. for the treatment of warts, is prohibited in Germany (AMK, 2001).

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

Studies in Animals

In vitro Studies

No data available.

In vivo Studies

In animals, 2-naphthol was absorbed after dermal application (Hemels, 1972a; Hemels, 1972b).

After subcutaneous administration, 2-naphthol was excreted in the urine, mainly in conjugated form, as the sulphate or glucuronide. Rats and pigs mainly excreted the glucuronide, while cats excreted up to 98 % of 2-naphthol as the sulphate (Capel et al., 1974).

In mice, the concentrations of 2-naphthol in lung, liver and kidney were highest within 1 to 2 hours after i.p. administration of 50 mg/kg bw, and then rapidly decreased. 2-Naphthol caused damage to Clara cells and a significant depletion of pulmonary GSH levels (reduced glutathione) at 12 hours after the administration of the compound (Honda et al., 1991).

Studies in Humans

In vitro Studies

No data available.

In vivo Studies

In humans, absorption through the skin was demonstrated following the use of 2-naphthol in a peeling paste for the treatment of acne. About 5 % of the applied dose (7.5 g paste containing 20 % 2-naphthol) was recovered after 24 hours in the urine. Plasma levels of 2-naphthol were significantly lower than the plasma levels of conjugated 2-naphthol. Tubular reabsorption and enterohepatic circulation may play a role for the long-lasting plasma levels (Hemels, 1972b). Substantially lower activities of glucuronyltransferase and sulphotransferase have been found in human fetuses as compared to adults, resulting in comparatively higher plasma levels of free 2-naphthol (Pacifici et al., 1990). The Human Cutaneous Permeability Coefficient Value (Kp) for 2-naphthol in aqueous solution (0.05 % w/v) was determined to be 0.0279 cm/h (Roberts et al., 1977).

Mean urinary 2-naphthol concentrations differed significantly between non-smokers and smokers, and were correlated with duration of smoking, and the daily amount smoked (Kim et al., 2001; Yang et al., 1999). No such difference was found in coke plant workers highly exposed to polycyclic hydrocarbons (PAHs) in the workplace air (Bienek, 1998). The intake of PAHs from the cigarette smoke seemed to be much lower than from the workplace air and by dermal contact.

Conclusion

2-Naphthol can be absorbed through the skin. Rapid conjugation with glucuronide and sulphate in the liver and renal excretion of the unchanged and conjugated forms seems to be the principal mechanism of elimination.

3.1.2 Acute Toxicity

Studies in Animals

Inhalation

In a study performed in accordance with OECD TG 403 a 4-hour inhalation LC_{50} of 2200 mg/m^3 was determined in rats of both sexes (Hoechst AG, 1993). Clinical signs included irregular breathing, reduced activity, impaired motility and reflexes at higher, not specified exposure levels. These animals showed also blood-stained nasal discharge, encrusted noses, corneal opacity and diarrhoea. All deaths occurred within 2 days after exposure. All surviving animals were free of symptoms on day 12 after exposure at the latest. At necropsy, Animals that were sacrificed at the end of the post-exposure observation period were free of pathological changes.

Dermal

For rats, the dermal LD_{50} value was greater than 10,000 mg/kg bw; no clinical signs were noted (BASF AG, 1975). In rabbits, the dermal LD_{50} value was reported to be greater than 10,000 mg/kg bw. No information on clinical signs is available for this study (Industrial Biotest Labs., 1973b). Since there is no information on the conduct of the studies, the reliability of these results cannot be evaluated.

Oral

2-Naphthol was tested for its acute toxicity in a study performed in accordance with the former OECD TG 401. In this study the oral LD_{50} was determined to be 1320 mg/kg bw in rats of both sexes (Hoechst AG, 1986). Clinical signs included reduced activity, prostration, irregular breathing, rough coat, nasal discharge, diarrhoea and closure of eyes. At doses levels $\geq$ 1600 mg/kg also tumbling, seizures and reduced reflex activity were observed. All surviving animals were free of symptoms on day 5 after exposure at the latest. At necropsy, vascular injection of the gastro-

intestinal tract, inflated stomachs, intestinal haemorrhage and brownish liquid in the urinary bladders were found. Animals that were killed at the end of the post-observation period were free of pathological changes.

Other Routes of Exposure

No data available.

Studies in Humans

Inhalation

No data available.

Dermal

No data available.

Oral

In four out of 79 farm workers that were treated for hookworm infection with 6 g of 2-naphthol (of unknown purity) for 3 days, haemolytic reactions resulting in severe anaemia, spleen and liver enlargement and haemoglobinuria were seen. Three out of the 4 workers had suffered from malaria beforehand (Smillie, 1920).

Other Routes of Exposure

No data available.

Conclusion

The acute oral LD_{50} in rats was determined as 1320 mg/kg bw in a study following the former OECD TG 401. Clinical signs included reduced activity, accelerated breathing, closure of eyes, nasal discharge and diarrhoea, and at exposure levels near to or exceeding the LD_{50} also tumbling, reduced reflexes and seizures. There is no adequate data to evaluate the acute dermal toxicity of 2-naphthol. The inhalation 4-hour-LC_{50} in rats was determined as 2200 mg/m^3 (aerosol). Clinical signs included irregular breathing, reduced activity, impaired motility and reflexes, nasal discharge, corneal opacity and diarrhoea.

3.1.3 Irritation

Skin Irritation

Studies in Animals

In a skin irritation study performed under semi-occlusive conditions according to OECD TG 404 with the moistened test substance, none of the animals showed any sign of irritation (4 hours exposure, 500 mg, moistened with 0.3 ml physiological saline, readings at 30 - 60 minutes, and 24, 48, and 72 hours after application). The Draize scores for erythema and edema were both "0"(Hoechst AG, 1986). Slight erythema, but no edema was observed in intact and abraded rabbit skin after 24 hours of exposure to the pulverized test material (Industrial Bio-Test Labs., 1973a).

Studies in Humans

No data vailable.

Eye Irritation

Studies in Animals

In an eye irritation study performed according to OECD TG 405, 2-naphthol (100 mg, undiluted) caused serious damage to the eyes of rabbits. 1 to 72 hours after application, swelling and conjunctivitis, corneal opacity (grade 1) and iritis (grade 1), as well as white ocular discharge were observed in all three animals. After 7 days one animal was free of symptoms, the other two showed slight to moderate conjunctivitis, one had iritis and white discharge. Both animals had corneal opacities with vascularization and conjunctivae were partly detached (Hoechst AG, 1986).

Studies in Humans

In workers occupationally exposed to 2-naphthol an increased incidence of dermatitis, conjunctivitis, and rhinitis was observed (Pyatnitskaya, 1973c).

Respiratory Tract Irritation

Studies in Animals

No data available.

Studies in Humans

No data available.

Conclusion

2-Naphthol was not irritating to the skin of rabbits in a test performed according to OECD TG 404. The chemical caused serious damage to the eyes of rabbits in a test performed in accordance with OECD TG 405 (corneal vascularization / opacity).

3.1.4 Sensitisation

Studies in Animals

Skin

2-Naphthol (99.9 %) was sensitising in a guinea pig maximization test performed in accordance with OECD TG 406. The animals were induced with 2 % 2-naphthol intradermally and with 25 % 2-naphthol in vaseline epicutaneously. Challenge was performed with the 25 % preparation in vaseline. All ten tested animals showed a positive reaction, whereas no effects were observed in the five control animals (Hoechst AG, 1992). The positive result is supported by a modified guinea pig maximization study, in which 2-naphthol was openly applied for challenge as a 1 % preparation in acetone. All 8 tested animals showed effects indicating skin sensitisation (Okada et al., 1985).

Respiratory Tract

No data available.

Studies in Humans

Skin

Contact dermatitis was reported in 21 out of 303 workers exposed to high concentrations of 2-naphthol (1 - 200 mg/m^3) (Dynnik et al., 1973). 2 out of 89 dermatitis patients showed a positive skin reaction when exposed to a 10 % preparation in olive oil (Baer et al., 1955), whereas in other

studies with limited numbers of subjects no sensitisation reactions were observed (Kozuka et al., 1980; Fujimoto et al., 1985).

Respiratory Tract

No data available.

Conclusion

2-Naphthol is a skin sensitiser, based on results from a guinea pig maximization test performed according to OECD TG 406. An increased incidence of contact dermatitis in exposed workers is reported in an old and poorly documented study**.**

3.1.5 Repeated Dose Toxicity

Studies in Animals

Inhalation

Poorly documented studies in rats involving repeated administration by the inhalation route for 1 - 4 months gave indications of an effect on the liver and kidneys. The earliest and most persistent sign was the change in kidney function, starting at exposure levels of 1 - 1.35 mg/m^3. Changes observed at 1.35 mg/m^3 in the 4 week study were reversible within 1 month after the end of the exposure. Concentration dependent disturbances in blood clotting and functional impairment of the liver and kidney with accompanying histopathological effects occurred at 10.1 and 1.35 mg/m^3. 0.45 mg/m^3 was considered as a threshold concentration by the authors (Prilipskii and Dynnik, 1971; Pyatnitzkaya et al., 1973a; 1973b).

Dermal

There were no data available with repeated dermal exposure. Poorly documented studies in dogs with subcutaneous administration for 9 months gave indications of an effect on the liver and kidneys. The earliest and most persistent sign was the change in kidney function, starting at exposure levels of 25 mg/kg bw/day s.c. (Prilipskii and Dynnik, 1971; Pyatnitzkaya et al., 1973a; 1973b).

Oral

In a 28 day gavage study in Wistar rats (0, 50, 150, 450 mg/kg bw/day), performed similar to the old OECD TG 407 (1981), 2-napththol had no influence on body weights, food consumption and behavior of the animals. The only clinical sign observed was brown staining of the coat in female animals from the high dose group. No treatment related effects were observed at the ophthalmic examinations. There were no changes in the hematological parameters. Males of the high dose group had significantly increased serum creatinine, sodium and calcium levels, together with a significant decrease in potassium levels at the end of the treatment period. All treated groups showed a slight and not dose-dependent increase in absolute and relative adrenal weights, the significance of this finding is unclear (Life Science Research-RTC, 1989).

LOAEL, rat (28d): 50 mg/kg bw/day (increased adrenal weights in both sexes).

Studies in Humans

Inhalation

Pathological changes in kidney function with dysury, nephrosis and inflammation of the urinary bladder, as well as higher incidences of gastric inflammation, chronic hepatitis and impairment of the nervous system were observed in workers exposed to 2-naphthol concentrations ranging between 1 and 200 mg/m^3 (Dynnik et al., 1973).

Dermal

No data available.

Oral

No data available.

Conclusion

After repeated administration to rats by the oral route for 28 days, there were indications of a possible effect on the adrenals in both sexes at dose levels of 50 mg/kg bw/day and above (increased relative and absolute adrenal weights). At 150 mg/kg bw/day, an increase in serum creatinine and changes in serum electrolytes were found in males, indicating an effect on the kidneys.

Poorly documented studies in dogs and rats involving repeated administration by the subcutaneous and inhalation route showed effects on the liver and kidneys. Concentration dependent disturbances in blood clotting and functional impairment of the liver and kidney with accompanying histopathological effects occurred at 10.1 and 1.35 mg/m^3.

3.1.6 Mutagenicity

Studies in Animals

In vitro Studies

2-Naphthol was not mutagenic in several Ames-tests using *Salmonella typhimurium* strains TA 98, TA100, TA 1535, TA 1537, TA 1538, G46, C3076, D3052, and *Escherichia coli* WP2uvrA, both in the presence and in the absence of metabolic activation (liver S-9 mix) and including cytotoxic concentrations (Probst et al., 1981; Purchase et al., 1978; Kawachi et al. 1980a; 1980b; Muzall and Cook, 1979; Florin et al., 1980). 2-Naphthol has however been found to exhibit mutagenic activity after UV irradiation at 25 °C in aqueous nitrite solution. There was evidence that the photochemical oxidation of 2-naphthol to 1,2-naphthoquinone as well as nitration plays an important role in the mutagen formation (Suzuki J et al., 1988).

It was tested positive in DNA repair tests with 4 strains of *Escherichia coli* and in one out of four *Bacillus subtilis* strains (Tanooka, 1977; Suter and Jaeger, 1982; Kawachi et al. 1980a; 1980b).

2-Naphthol did not induce unscheduled DNA synthesis in rat hepatocytes in vitro (Probst et al., 1981).

In vivo Studies

A micronucleus assay was conducted according to the OECD TG 474 under GLP (MHLW, Japan, 2005) Male BDF1 mice were given 2-naphthol by gavage at 62.5 - 250 mg/kg bw/day for two days. 2-Naphthol showed no induction of micronuclei in bone marrow polychromatic erythrocytes.

Studies in Humans

No data available.

Conclusion

2-Naphthol was not mutagenic in several Ames tests both in the absence and in the presence of metabolic activation, even at cytotoxic concentrations. Inconsistent results have been observed in bacterial DNA repair tests, but it did not induce unscheduled DNA synthesis in rat hepatocytes in a test performed to current standards. 2-Naphthol was not tested for its potential to induce chromosomal aberrations *in vitro.*

In an *in vivo* micronucleus assay, 2-naphthol was reported to be without effects on bone marrow cells of mice. 2-Naphthol is not mutagenic *in vivo*.

3.1.7 Carcinogenicity

In vitro Studies

Growth inhibition and cell transformation to a squamous morphology was observed in response to 2-naphthol exposure (10 - 100 uM) in cultured bronchial epithelial cells. The responses were observed at subtoxic concentrations and removal of the exposures was followed by renewed proliferation, perhaps by a subpopulation of resistant cells. Of the phenolic compounds tested, catechol was the most active. 2-Naphthol had a potency intermediate to catechol and phenol (Palmatier et al., 1997).

In vivo Studies in Animals

Inhalation

No data available.

Dermal

In limited 12- and 21-week studies, 20 % solutions of 2-naphthol in acetone or ethanol had no tumor promoting activity on mouse skin (Boutwell and Bosch, 1959).

Oral

No data available.

Studies in Humans

No data available.

Conclusion

There are no adequate data available for the evaluation of the carcinogenic potential of 2-naphthol.

3.1.8 Toxicity for Reproduction

Studies in Animals

Effects on Fertility and Development

In a one-generation study in Sprague-Dawley rats, performed in accordance with OECD TG 415 (Environmental Health Bureau, 2000), males were dosed by gavage with 2-naphthol (purity 99.6 %) for 10 weeks prior to mating, during the mating period and until the day before necropsy (in total,

98 days) and females for 2 weeks prior to mating, during mating and gestation and until day 20 of lactation (0; 10; 40; 160 mg/kg bw/day). The administration of the test substance had no effect on reproductive performance. No adverse effect of the test substance was observed on pairing days until conception and number of vaginal estrous during the mating period. Furthermore, no abnormality was found in delivery, on gestation index and gestation length. According to the authors of the study, 160 mg/kg bw/day could however suppress nursing behaviour, since 2-naphthol was shown to depress activity in dams (NOEL for male reproductive toxicity: 160 mg/kg bw/day; NOEL for female reproductive toxicity: 40 mg/kg bw/day)

After dosing, transient salivation was noted in males of all dose groups, and in females of the mid- and high dose groups. In mid- and high dose males and females, nasal discharge and in high dose males lacrimation was observed. While body weight gain was not clearly affected, food consumption was decreased in females at the beginning of the gestation period in the mid- and high-dose groups and after day 4 of lactation in the high dose group. A decrease in locomotor activity was also noted in females of the mid- and high-dose groups.

At necropsy, thickening of the mucosa of the forestomach was observed in male animals of the mid- and high-dose group. Histopathological examination revealed hyperplasia of the forestomach squamous epithelium in these animals. No histopathological changes were found in the pituitary glands, testes, epididymides, coagulating glands, seminal vesicles, prostates, ovaries, uterus, cervix and vagina and in the stomach of females. The LOEL for systemic toxicity in males was 10 mg/kg bw (salivation), the NOEL for systemic toxicity in females was 10 mg/kg bw/day (salivation, nasal discharge, reduced food consumption, decreased locomotor activity at 40 mg/kg bw/day).

Administration of the test substance did not affect general condition, including behaviour of the offspring. A decreased birth index was noted in the high dose group, but this was not statistically significant. In the high-dose group, the viability index was slightly reduced at day 4 after birth. There was no effect on sex ratio and weaning index. Decreased body weights were found in the female pups in the high-dose group at day 21 after birth (minus 14 % versus controls). Similar, but less pronounced effects were found in male pups. No effects on body weight were seen in the low- and mid-dose groups (NOEL for toxicity to the offspring: 40 mg/kg bw/day).

At the morphological examination of the offspring, minor malformations and variations were seen scattered among groups, including the controls. Since no significant differences in the incidence of morphological changes and no dose relationships were observed, these effects were judged as chance events (NOEL for teratogenicity: 160 mg/kg bw/day).

Studies in Humans

Effects on Fertility

No data available.

Developmental Toxicity

No data available.

Conclusion

2-Naphthol was tested for its reproductive toxicity in a one-generation study according to OECD TG 415. The administration of the test substance had no adverse effect on the reproductive abilities of the parental generation. No teratogenic effects were observed.

No Effect Levels (NOELs):

NOEL for male reproductive toxicity: 160 mg/kg bw/day (highest tested dose).

NOELs for female reproductive toxicity and for toxicity to the offspring: 40 mg/kg bw/day each. (160 mg/kg bw/day may suppress nursing; reduced body weights and reduced viability were seen in the offspring at 160 mg/kg bw/day).

The LOEL for systemic toxicity in males was 10 mg/kg bw/day (salivation), the NOEL for systemic toxicity in females was 10 mg/kg bw/day (nasal discharge, reduced food consumption, decreased locomotor activity and salivation at 40 mg/kg bw/day).

3.2 Initial Assessment for Human Health

2-Naphthol can be absorbed through the skin. Rapid conjugation with glucuronide and sulphate in the liver and renal excretion of the unchanged and conjugated forms seems to be the principal mechanism of elimination.

The acute oral LD_{50} in rats was determined as 1320 mg/kg bw in a study following OECD TG 401. Clinical signs included reduced activity, accelerated breathing, closure of eyes, nasal discharge and diarrhoea, and at exposure levels near to or exceeding the LD_{50} also tumbling, reduced reflexes and seizures.

The inhalation 4-hour-LC_{50} in rats was determined as 2200 mg/m^3 (aerosol; OECD TG 403). Clinical signs included irregular breathing, reduced activity, impaired motility and reflexes, nasal discharge, corneal opacity and diarrhea.

2-Naphthol was not irritating to the skin of rabbits in a test performed according to OECD TG 404, but caused serious damage to the eyes of rabbits in a study in accordance with OECD TG 405 (corneal vascularization/opacity).

2-Naphthol is a skin sensitiser, based on results from a guinea pig maximization test [OECD TG 406]. An increased incidence of contact dermatitis in exposed workers is reported in an old and poorly documented study.

After repeated administration to rats by the oral route for 28 days, there were indications of a possible effect on the adrenals in both sexes at dose levels of 50 mg/kg bw/day and above (increased relative and absolute adrenal weights). At 150 mg/kg bw/day, an increase in serum creatinine and changes in serum electrolytes were found in males, indicating an effect on the kidneys. Poorly documented studies in dogs and rats involving repeated administration by the subcutaneous and inhalation route showed effects on the liver and kidneys. Concentration dependent disturbances in blood clotting and functional impairment of the liver and kidney with accompanying histopathological effects occurred at 10.1 and 1.35 mg/m^3.

2-Naphthol was not mutagenic in several Ames tests both in the absence and in the presence of metabolic activation, even at cytotoxic concentrations. Inconsistent results have been observed in bacterial DNA repair tests, but it did not induce unscheduled DNA synthesis in rat hepatocytes in a test performed according to current standards. 2-Naphthol was not tested for its potential to induce chromosomal aberrations *in vitro*. In an *in vivo* micronucleus assay of 2-naphthol, no evidence of genotoxicity was found. These data indicate that 2-naphthol is not mutagenic *in vivo.*

There are no adequate data available for the evaluation of the carcinogenic potential of 2-naphthol.

2-Naphthol was tested for its reproductive toxicity in a one-generation study according to OECD TG 415. The administration of the test substance had no adverse effect on the reproductive abilities of the parental generation. No teratogenic effects were observed (NOEL for male reproductive toxicity: 160 mg/kg bw/day (highest tested dose); NOELs for female reproductive toxicity and for toxicity to the offspring: 40 mg/kg bw/day each). (160 mg/kg bw/day may suppress nursing; reduced body weights and reduced viability was seen in the offspring at 160 mg/kg bw/day). The LOEL for systemic toxicity in males was 10 mg/kg bw/day (salivation), the NOEL for systemic

toxicity in females was 10 mg/kg bw/day (nasal discharge, reduced food consumption, decreased locomotor activity and salivation at 40 mg/kg bw/day).

In workers exposed to 2-naphthol an increased incidence of dermatitis, conjunctivitis, and rhinitis have been reported in poorly documented studies. In addition, changes in kidney function, and an increased incidence in chronic hepatitis and impairment of the nervous system were reported from workers who were also exposed to a variety of other chemicals.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

Acute Toxicity Test Results

The following valid test results with aquatic organisms are available:

a) fish

Micropterus salmoides LC_{50} = 1.77 mg/l (7 d)
(embryo-larval test, flow through system, average hatching time 3d, posthatching 4 d, measured concentration) (Black et al., 1983)

Oncorhynchus mykiss LC_{50} = 0.07 mg/l (27 d)
NOEC = 0.001 mg/l (27d)
(embryo-larval test, flow through system, average hatching time 23 d, posthatching 4 d, measured concentration) (Black et al., 1983)

Gadus morrhua LC_{50} > 3 mg/l (96 h)
(static test with fish eggs, starting during the first day after fertilization, measured concentration) (Falk-Petersen et al., 1985))

Pimephales promelas LC_{50} = 3.46 mg/l (96 h)
(static, measured concentration) (Millemann et al., 1984)

The lowest effect value found in short-term tests is the 96h-LC_{50} of 3.46 mg/l for *Pimephales promelas*. This study is therefore selected as key study.

Only one NOEC obtained in a long-term study is available. This NOEC of 1 µg/l was found by Black et al. in an embryo-larval test with *Oncorhynchus mykiss*. However, for several substances it became obvious that the effect values found by Black et al. in such tests are usually very low compared to effect values found by other authors (e.g. for the EU priority substance toluene Black et al. reported a 27d-EC_{10} of 2.9 µg/l while all other available long-term fish tests, using partly the same test species, found NOEC-values in the range of 1.4 to 4.7 mg/l). No explanation for these large discrepancies could be found. A careful examination of the entire information provided by Black et al. gave no plausible reason for the inconsistency of the data. However, as it was not possible to reproduce the effect values found by Black and his co-workers, it is proposed not to use these data for the further effects assessment.

b) invertebrates

Daphnia magna EC_{50} = 3.54 mg/l (48 h)

(effect: immobilisation, measured concentration) (Millemann et al., 1984))

Gammarus minus LC_{50} = 0.85 mg/l (48 h)
(effect: immobilisation, measured concentration) (Millemann et al., 1984)

Chironomus tentans LC_{50} = 4.32 mg/l (48 h)
(measured concentration) (Millemann et al., 1984)

Physa gyrina LC_{50} = 24.7 mg/l (48 h)
(measured concentration) (Millemann et al., 1984)

Strongylocentrotus droebachiensis EC_{50} = 1.9 mg/l (96 h)
(test with sea-urchin eggs, starting the first day after fertilization, measured concentration) (Falk-Petersen et al., 1985).

The most sensitive invertebrate species was *Gammarus minus* with an 96h-EC_{50} of 0.85 mg/l. Therefore, this study was selected as key study.

c) algae

Microcystis aeruginosa EC_{20} = 0.75 mg/l (4 h)
(effect: reduction of photosynthesis, nominal concentration) (Giddings, 1980)

Selenastrum capricornutum EC_{20} = 4 mg/l (4 h)
(effect: reduction of photosynthesis, nominal concentration) (Giddings, 1980)

Natural algal community EC_{20} = 1 mg/l (4 h)
(effect: reduction of photosynthesis, nominal concentration) (Giddings, 1980)

Nitzschia palea EC_{50} = 6.3 mg/l (4 h)
(effect: reduction of assimilation rate, measured concentration) (Millemannet al., 1984)

Selenastrum capricornutum EC_{50} = 18.8 mg/l (4 h)
(effect: reduction of assimilation rate, measured concentration) (Millemann et al., 1984)

Selenastrum capricornutum $EC_{50} \approx$ 4 mg/l
(2 tests: static and dynamic bioassay; effect: growth rate during exponential growth phase, exposure time not given, nominal concentration) (Klaine et al., 1983)

No standard test on green algae is available for 2-naphthol. However, the entiety of the available non-standard studies seems sufficient at the present stage of the hazard assessment. QSAR may be used to support the validity of the present data for algae. Using the EPIWIN model results in an 96h-EC_{50} for green algae of 12.9 mg/l. This supports the assumption that green algae are not likely to be the most sensitive species in short-term tests.
Only for two algae species an EC_{50} is given. Therefore, the study reporting the lowest EC_{50}-value (*Nitschia palea*: 4h-EC_{50} = 6.3 mg/l) is chosen as key study.

Chronic Toxicity Test Results

Only one NOEC obtained in a long-term study is available. This NOEC of 1 µg/l was found by Black et al. in an embryo-larval test with *Oncorhynchus mykiss*. However, for several substances it became obvious that the effect values found by Black et al. in such tests are usually very low compared to effect values found by other authors (e.g. for the EU priority substance toluene Black et al. reported a 27d-EC_{10} of 2.9 µg/l while all other available long-term fish tests, using partly the same test species, found NOEC-values in the range of 1.4 to 4.7 mg/l). No explanation for these large discrepancies could be found. A careful examination of the entire information provided by Black et al. gave no plausible reason for the inconsistency of the data. However, as it was not possible to reproduce the effect values found by Black and his co-workers, it is proposed not to use these data for the further effects assessment.

Toxicity to Microorganisms

There are no tests with microorganisms available that can be used for an environmental hazard assessment of 2-naphthol, as they are either performed with pathogenic organisms or under anaerobic conditions.

Derivation of PNECaqua

If the effect values reported by Black et al. are disregarded, there are only short-term tests with 2-naphthol available. The most-sensitive species was the crustacean *Gammarus minus* with a 48h-EC_{50} of 0.85 mg/l. For the derivation of the PNECaqua an assessment factor of 1000 is adequate as only short-term tests are available. Therefore, the **PNECaqua is 0.85 µg/l.**

4.2 Terrestrial Effects

No effect values for terrestrial organisms are available.

4.3 Other Environmental Effects

There is only one test on *Agelaius phoeniceus* available: Based on food consumption over a 18h period, a $LD_{50} \geq 100$ mg/l was estimated (Schafer et al., 1983).

4.4 Initial Assessment for the Environment

Naphthol is readily biodegradable as shown in a MITI test according to OECD 301C with non-adapted inoculum. A biodegradation of 68 % after 14 days was found. There is no information on the degradation kinetic. The measured log K_{OW} in the range of 2.01 to 2.84 does not indicate a significant potential for bio- or geoaccumulation. With a fugacity model (Mackay I) the following distribution can be predicted: hydrosphere: 83 %, atmosphere: 8 %, soil: 4.5 % and sediment: 4.5 %. The hydrosphere is therefore the target compartment for this substance. In water solution, photodegradation has been observed, but the half-life under environmental conditions was not estimated. The calculated half-life due to photochemical-oxidative degradation in the atmosphere by OH-radicals is about 2 hours.

For 2-naphthol there are short-term tests with fish, invertebrates and algae available. The lowest effects values from the short-term tests are:
Pimephales promelas: 96h-LC_{50} = 3.46 mg/l, *Gammarus minus*: 48h-EC_{50} = 0.85 mg/l, *Nitzschia palea*: 4h-EC_{50} = 6.3 mg/l. With an assessment factor of 1000 a PNECaqua of 0.85 µg/l was derived from the 48h-EC_{50} for the most sensitive species, *Gammarus minus.*

5 RECOMMENDATIONS

ENVIRONMENT

The substance is a candidate for further work. Little information is available about releases into the environment from production and processing sites and from the direct use of the substance. However, this information indicates that significant releases into the environment may occur. In addition, the relevance of releases into the terrestrial compartment from the metabolisation of the herbicide naproanilide should be clarified. Therefore, an exposure assessment is recommended. This recommendation is based on the high toxicity of 2-naphthol to aquatic organisms. A PNECaqua of 0.85 µg/l was derived from the available short-term data. Dependent on the exposure situation further tests with aquatic and/or terrestrial organisms may be required.

HUMAN HEALTH

The chemical is currently of low priority for further work based on its low hazard profile. It is noted that the chemical can cause serious eye damage and is a skin sensitiser.

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I U C L I D

Data Set

Existing Chemical	:	ID: 135-19-3
CAS No.	:	135-19-3
EINECS Name	:	2-naphthol
EC No.	:	205-182-7
TSCA Name	:	2-Naphthalenol
Molecular Formula	:	C10H8O

Producer related part

Company	:	BUA - TU München
Creation date	:	02.08.2005

Substance related part

Company	:	BUA - TU München
Creation date	:	02.08.2005
Status	:	
Memo	:	
Printing date	:	09.02.2006
Revision date	:	02.08.2005
Date of last update	:	09.02.2006
Number of pages	:	118
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
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 APPLICANT AND COMPANY INFORMATION

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type :
Substance type : organic
Physical status : solid
Purity : >= 99 % w/w
Colour :
Odour :

Source : BUA - TU München Freising

(1)

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

(2)-Naphtol

Source : BUA - TU München Freising

.beta.-Naphthol

Source : BUA - TU München Freising

.beta.-Naphthyl alcohol

Source : BUA - TU München Freising

2-Hydroxynaphthalene

Source : BUA - TU München Freising

2-Hydroxynaphthalin

Source : BUA - TU München Freising

2-Naphthalenol

Source : BUA - TU München Freising

2-Naphthalenol (9Cl)

Source : BUA - TU München Freising

2-Naphthalinol

Source : BUA - TU München Freising

2-Naphthol

Source : BUA - TU München Freising

2-Naphthol (8Cl)

Source : BUA - TU München Freising

2-Naphthol,2-Hydroxy-Naphthalene

Source : BUA - TU München Freising

Azogen Developer A

Source : BUA - TU München Freising

B-Naphthol

Source : BUA - TU München Freising

Beta naphthol

Source : BUA - TU München Freising

beta-Hydroxynaphthalene

Source : BUA - TU München Freising

beta-MONOXYNAPHTHALENE

Source : BUA - TU München Freising

beta-Naftol

Source : BUA - TU München Freising

beta-Naphthol

Source : BUA - TU München Freising

beta-Naphthol DS

Source : BUA - TU München Freising

beta-Naphthol fluessig

Source : BUA - TU München Freising

beta-Naphthyl alcohol

Source : BUA - TU München Freising

beta-NAPHTHYL HYDROXIDE

Source : BUA - TU München Freising

C.I. 37500

Source : BUA - TU München Freising

C.I. Azoic Coupling Component 1

Source : BUA - TU München Freising

C.I. Developer 5

Source : BUA - TU München Freising

Developer A

Source : BUA - TU München Freising

Developer AMS

Source : BUA - TU München Freising

Developer BN

Source : BUA - TU München Freising

Developer NA

Source : BUA - TU München Freising

Developer sodium

Source : BUA - TU München Freising

Isonaphthol

Source : BUA - TU München Freising

Naphthol B

Source : BUA - TU München Freising

ß-Naphthol

Source : BUA - TU München Freising

1.3 IMPURITIES

1.4 ADDITIVES

1.5 TOTAL QUANTITY

Quantity : ca. 100000 - tonnes produced in

Remark : worldwide production capacity.
China, India, Japan, Italy and some east European countries are the main production countries.
In Japan there are three production factories with the total capacity of 10,000 tons per year. India has 7 factories of beta-naphthol production with the capacity of 10,000 tons per year. Italy has one factory with the capacity of 20,000 tons per year. In former Russia, the production capacity is around 14,000 tons per year. In China, the production capacity has reached 40,000 tons per year. Germany and the United States have stopped their production.

Source : BUA - TU München Freising

(2)

1.6.1 LABELLING

Labelling : as in Directive 67/548/EEC
Specific limits : no data
Symbols : Xn, N, ,
Nota : C, ,
R-Phrases : (20/22) Harmful by inhalation and if swallowed
(50) Very toxic to aquatic organisms
S-Phrases : (2) Keep out of reach of children
(24/25) Avoid contact with skin and eyes
(61) Avoid release to the environment. Refer to special instructions/Safety data sets

Source : BUA - TU München Freising

1.6.2 CLASSIFICATION

Classified : as in Directive 67/548/EEC
Class of danger : corrosive
R-Phrases : (20/22) Harmful by inhalation and if swallowed
Specific limits :

Source : BUA - TU München Freising

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

Source : BUA - TU München Freising

1.6.3 PACKAGING

1.7 USE PATTERN

Remark : 2-Naphthol is mainly used as intermediate for the production of dyestuffs. Further products are pharmaceuticals, fungicides, insecticide and odor agents. The substance is also used as an antioxidant for rubber and plastic, grease and lubricants.
Source : BUA - TU München Freising

(3)

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

Remark : 2-naphthol is a constituent of mainstream non-filter cigarette smoke (0.54 µg/cigarette)
Source : BUA - TU München Freising
Reliability : (4) not assignable
secondary quotation

(4)

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

Type of search : External
Chapters covered : 5
Date of search : 12.05.2002

Remark : Search for CAS number in BIOS, TOXLINE, MEDLINE and TSCATS
Source : BUA - TU München Freising

1.13 REVIEWS

Memo : Toxicological Evaluation. 2-Naphthol.

Source : BUA - TU München Freising
(5)

Memo : review

Source : BUA - TU München Freising
(6)

2.1 MELTING POINT

Value : = 121 °C

Remark : solidification point
Source : BUA - TU München Freising
Reliability : (4) not assignable
safety data sheet
Flag : Critical study for SIDS endpoint

(7) (8) (9)

Value : = 123 °C

Source : BUA - TU München Freising
Reliability : (4) not assignable
data from chemicals catalogue (not specified)

(10)

2.2 BOILING POINT

Value : = 296 °C at 1013 hPa

Source : BUA - TU München Freising
Reliability : (4) not assignable
safety data sheet
Flag : Critical study for SIDS endpoint

(8) (9)

Value : = 400 °C at
Decomposition : yes
Method : other: DTA
Year :
GLP :
Test substance :

Source : BUA - TU München Freising
Test condition : 10 K/min
Reliability : (4) not assignable
company product information

(7)

Value : > 500 °C at
Decomposition : yes
Method : other: DTA
Year :
GLP :
Test substance :

Source : BUA - TU München Freising
Test condition : 10 K/min
Reliability : (4) not assignable
company product information

(8) (9)

2.3 DENSITY

Type : density
Value : = 1.06 g/cm³ at 135 °C

Source : BUA - TU München Freising
Reliability : (4) not assignable
safety data sheet

(8) (9)

Type : bulk density
Value : ca. 600 kg/m3 at °C

Source : BUA - TU München Freising
Reliability : (4) not assignable
safety data sheet

(9)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : < .1 hPa at 15 °C

Source : BUA - TU München Freising
Reliability : (4) not assignable
safety data sheet

(8)

Value : < .1 hPa at 20 °C

Source : BUA - TU München Freising
Reliability : (4) not assignable
safety data sheet

(9)

Value : = 4 hPa at 25 °C

Source : BUA - TU München Freising
Reliability : (4) not assignable

(11)

Value : = 1.06 hPa at 100 °C

Source : BUA - TU München Freising
Reliability : (4) not assignable
safety data sheet

(8) (9)

Remark : No experimental data at 20 degree C available. The extrapolation of vapour pressures at higher temperatures range 145 - 300 degree C (Weast: Handbook of Chemistry and Physics; 64th ed.) amount to the following data:
0.014 hPa at 20 degree C
0.02 hPa at 25 degree C

Source : BUA - TU München Freising
Reliability : (4) not assignable
extrapolation from data given in handbook
Flag : Critical study for SIDS endpoint

(12)

2.5 PARTITION COEFFICIENT

Partition coefficient :
Log pow : = 2.01 at °C
pH value :
Method : other (measured): HPLC
Year :
GLP :
Test substance :

Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint

(13)

Partition coefficient : octanol-water
Log pow : = 2.585 at °C
pH value :
Method : other (calculated)
Year :
GLP :
Test substance :

Method : log Pow was calculated using the CHEMICALC system (Suzuki T and Kudo Y, 1990: J. Comput.-Aided Mol Design 4, 155-198)
Source : BUA - TU München Freising
Reliability : (2) valid with restrictions

(10)

Partition coefficient :
Log pow : = 2.65 at °C
pH value :
Method : other (calculated): Leo, Hansch: Medchem-Software CLOGP3, Release 3.42, PomonaCollege, Clermont CA
Year : 1986
GLP :
Test substance :

Source : BUA - TU München Freising
Reliability : (2) valid with restrictions

(14)

Partition coefficient :
Log pow : = 2.7 at °C
pH value :
Method : other (measured): shake-flask method
Year :
GLP :
Test substance :

Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint

(15)

Partition coefficient :
Log pow : = 2.84 at °C
pH value :
Method : other (measured): Shake-flask
Year :
GLP :
Test substance :

Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint

(13)

Partition coefficient : octanol-water
Log pow : = 2.84 at °C
pH value :

Remark : reported value: Kow = 691.83
Source : BUA - TU München Freising
Reliability : (4) not assignable
secondary citation

(16)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in :
Value : = .9 g/l at 31 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Source : BUA - TU München Freising
Reliability : (4) not assignable
safety data sheet

(8) (9)

Solubility in :
Value : = .6 g/l at 25 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Source : BUA - TU München Freising
Reliability : (4) not assignable
company product information
Flag : Critical study for SIDS endpoint

(7)

Solubility in :

Value : = .5 g/l at 15 °C
pH value : ca. 7
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Source : BUA - TU München Freising
Reliability : (4) not assignable
safety data sheet

(8)

Solubility in :
Value : = .5 g/l at 15 °C
pH value : ca. 7
concentration : .8 g/l at 25 °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Source : BUA - TU München Freising
Reliability : (4) not assignable
safety data sheet
Flag : Critical study for SIDS endpoint

(17)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value : = 158 °C
Type :

Source : BUA - TU München Freising
Reliability : (4) not assignable
safety data sheet

(8) (9)

Value : = 160 °C
Type :

Source : BUA - TU München Freising
Reliability : (4) not assignable
company product information

(7)

2.8 AUTO FLAMMABILITY

Value : = 550 °C at

Remark : ignition temperature
Source : BUA - TU München Freising

Reliability : (4) not assignable
safety data sheet

(8) (9)

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

Acid-base constant : pKa = 9.51

Source : BUA - TU München Freising
Reliability : (4) not assignable

(18)

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	water
Light source	:	Sun light
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
Deg. product	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	no data
Remark	:	2-naphthol was subsequently hydroxylated to naphthalenediols and then oxidized to naphthoquinone.
Source	:	BUA - TU München Freising
Test condition	:	The aqueous solution was exposed to sunlight for 6 h per day for 2 days. The photodegradation was investigated under laboratory conditions using C14-labeled (at the naphthalene-ring) compounds. During: the photodegradation of the herbicide naproanilide, the radioactivity of the degradation product 2-naphthol sank from 4.3 % after 1 h of exposure to sunlight to 0.3 % after 12 h of exposure.
Test substance	:	2-Naphthol
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

(19)

INDIRECT PHOTOLYSIS

Sensitizer	:	OH
Conc. of sensitizer	:	500000 molecule/cm³
Rate constant	:	= .000000000200036 cm³/(molecule*sec)
Degradation	:	= 50 % after .1 day(s)
Deg. product	:	
Method	:	other (calculated): according to Atkinson
Year	:	1988
GLP	:	
Test substance	:	other TS
Source	:	BUA - TU München Freising
Test substance	:	2-Naphthol
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

(20)

3.1.2 STABILITY IN WATER

Remark	:	No data available; hydrolytic degradation unlikely
Source	:	BUA - TU München Freising

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

Type of measurement	:	background concentration

Media : surface water
Concentration :
Method :

Remark : 2-naththol was identified 1975 qualitatively in 6 of 21 analysed extracts from the river Rhein and Main (Germany) respectively.
Source : BUA - TU München Freising

(21)

Type of measurement : concentration at contaminated site
Media : other: Water and soil of a paddy field
Concentration :
Method :

Remark : 2-naphthol was identified as one of the photodegradationproducts of the herbicides naproanilide and NOP in aqeuous solution, in surface water of flooded soil and the soil layer of paddy fields under sunlight and ultraviolet light.
Source : BUA - TU München Freising
Test condition : The photodegradation was investigated under laboratory conditions using C14-labeled (at the naphthalene-ring) compounds.

(19)

Type of measurement : concentration at contaminated site
Media : ground water
Concentration :
Method :

Remark : 2-naphthol was identified qualitatively in groundwater collected near the Hazardous waste side near Pensacola, FL (USA).
Source : BUA - TU München Freising

(22)

Type of measurement : concentration at contaminated site
Media : other: Waste water of the oil shale processing industry
Concentration :
Method :

Remark : 2-naphthol was qualitatively identificated in the waste water of the oil shale processing industry.
Source : BUA - TU München Freising

(23)

Type of measurement : concentration at contaminated site
Media : biota
Concentration :
Method :

Remark : 2-naphthol was qualitatively identificated in rice irrigated with waste water of the oil shale processing industry.
Source : BUA - TU München Freising
Test condition : The contend of total steam-volatile phenols in the water was 50 ppm and 250 ppm in the last two irrigation times. No further information about the testperiod and applicationrates.

(23)

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	fugacity model level I
Media	:	
Air	:	% (Fugacity Model Level I)
Water	:	% (Fugacity Model Level I)
Soil	:	% (Fugacity Model Level I)
Biota	:	% (Fugacity Model Level II/III)
Soil	:	% (Fugacity Model Level II/III)
Method	:	other: Version 2.1
Year	:	
Remark	:	Input values: log Kow: 2.84; water solubility: 700 mg/l; vapor pressure: 1.4 Pa
Result	:	water: 83 % air: 8 % soil: 4.5 % sediment: 4.5 %
Source	:	BUA - TU München Freising
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	activated sludge, non-adapted
Concentration	:	100 mg/l related to Test substance related to
Contact time	:	
Degradation	:	= 68 (±) % after 14 day(s)
Result	:	readily biodegradable
Deg. product	:	
Method	:	OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"
Year	:	
GLP	:	no data
Test substance	:	other TS
Remark	:	no information about degradation kinetic
Source	:	BUA - TU München Freising
Test substance	:	2-Naphthol
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

(24)

Type	:	aerobic
Inoculum	:	activated sludge, industrial, adapted
Concentration	:	75 mg/l related to COD (Chemical Oxygen Demand) related to

Contact time :
Degradation : = 20 (±) % after 24 hour(s)
Result :
Deg. product :
Method : other: Activated sludge simulation test
Year :
GLP : no data
Test substance : other TS

Remark : About 6 % of the COD was removal by evaporisation during the test.
Source : BUA - TU München Freising
Test condition : Temperature: 25 degree C; aerated
Test substance : 2-Naphthol
Reliability : (2) valid with restrictions

(25)

Type : aerobic
Inoculum : activated sludge, industrial, adapted
Concentration : 36 mg/l related to DOC (Dissolved Organic Carbon) related to
Contact time :
Degradation : = 8 (±) % after 24 hour(s)
Result :
Deg. product :
Method : other: Activated sludge simulation test; fill-and-draw-type unit
Year :
GLP : no data
Test substance : other TS

Remark : About 7 % of the DOC was removal by evaporisation during the test.
Source : BUA - TU München Freising
Test condition : Temperature: 25 degree C; aerated
Test substance : 2-Naphthol
Reliability : (2) valid with restrictions

(25)

Type : aerobic
Inoculum : activated sludge, non-adapted
Concentration : 100 mg/l related to Test substance related to
Contact time :
Degradation : ca. 40 (±) % after 250 hour(s)
Result :
Deg. product :
Method : other: Biodegradation test in an electrolytic respirometer
Year :
GLP : no data
Test substance : other TS

Remark : Lag time: 155 - 180 hours; degradation measured as BOD/ThOD
Source : BUA - TU München Freising
Test condition : Temperature: 20 +/- 1 degree C; pH-value: 7 +/-; concentration of activated sludge: 30 mg/l
Test substance : 2-Naphthol
Reliability : (2) valid with restrictions

(26) (27)

Type : aerobic
Inoculum : activated sludge, industrial
Concentration : 770 mg/l related to DOC (Dissolved Organic Carbon)

related to
Contact time :
Degradation : = 90 (±) % after 13 day(s)
Result :
Kinetic of testsubst. : 3 hour(s) < 10 %
%
5 day(s) = 30 %
10 day(s) = 70 %
%
Deg. product :
Method : other: Zahn-Wellens-Test
Year : 1987
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Source : BUA - TU München Freising
Reliability : (4) not assignable
only test results available
(28)

Type : aerobic
Inoculum : activated sludge, industrial
Concentration : 860 mg/l related to DOC (Dissolved Organic Carbon)
related to
Contact time :
Degradation : = 92 (±) % after 15 day(s)
Result :
Kinetic of testsubst. : %
%
5 day(s) = 71 %
10 day(s) = 91 %
%
Deg. product :
Method : other: Zahn-Wellens-Test
Year : 1980
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Source : BUA - TU München Freising
Reliability : (4) not assignable
only test results available
(29)

Type : aerobic
Inoculum : activated sludge, adapted
Concentration : 100 mg/l related to Test substance
related to
Contact time :
Degradation : = 99.83 (±) % after 5 day(s)
Result :
Deg. product :
Method : other: slightly modified OECD system (confirmatory Test Procedure)
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : The activated sludge was cultivated on dairy-effluent and adapted to meat extract-peptonebroth. During the investigation the concentration of 2-naphthol was increased in the feed as compatible in the biodegradation.
Degradation is related to removal

Source : BUA - TU München Freising
Test condition : Adaptiontime: 100 d; pH: 7 - 8; BOD measurement; Retention time: 48 h
Reliability : (2) valid with restrictions
(30)

Type : aerobic
Inoculum : activated sludge, adapted
Concentration : 800 mg/l related to Test substance related to
Contact time :
Degradation : = 99.88 (±) % after 5 day(s)
Result :
Deg. product :
Method : other: slightly modified OECD system (confirmatory Test Procedure)
Year :
GLP : no data
Test substance : other TS

Remark : The activated sludge was cultivated on dairy-effluent and adapted to meat extract-peptonebroth. During the investigation the concentration of 2-naphthol was increased in the feed as compatible in the biodegradation. Degradation is related to removal.
Source : BUA - TU München Freising
Test condition : Adaptiontime: 150 d; pH: 7 - 8; BOD measurement; Retention time: 48 h
Test substance : 2-Naphthol
Reliability : (2) valid with restrictions
(30)

Type : aerobic
Inoculum : activated sludge, adapted
Concentration : 1000 mg/l related to Test substance related to
Contact time :
Degradation : > 99.9 (±) % after 5 day(s)
Result :
Deg. product :
Method : other: slightly modified OECD system (confirmatory Test Procedure)
Year :
GLP : no data
Test substance : other TS

Remark : The activated sludge was cultivated on dairy-effluent and adapted to meat extract-peptonebroth. During the investigation the concentration of 2-naphthol was increased in the feed as compatible in the biodegradation. Degradation is related to removal.
Source : BUA - TU München Freising
Test condition : Adaptiontime: 160 d; pH: 7 - 8; BOD measurement; Retention time: 48 h
Test substance : 2-Naphthol
Reliability : (2) valid with restrictions
(30)

Type : aerobic
Inoculum : activated sludge, adapted
Concentration : 300 mg/l related to Test substance related to
Contact time :

Degradation	:	= 99.98 (±) % after 5 day(s)
Result	:	
Deg. product	:	
Method	:	other: slightly modified OECD system (confirmatory Test Procedure)
Year	:	
GLP	:	no data
Test substance	:	other TS
Remark	:	The activated sludge was cultivated on dairy-effluent and adapted to meat extract-peptonebroth. During the investigation the concentration of 2-naphthol was increased in the feed as compatible in the biodegradation. Degradation is related to removal.
Source	:	BUA - TU München Freising
Test condition	:	Adaptiontime: 130 d; pH: 7 - 8; BOD measurement; Retention time: 48 h
Test substance	:	2-Naphthol
Reliability	:	(2) valid with restrictions

(30)

Type	:	anaerobic
Inoculum	:	other: Primary digesting sludge
Concentration	:	50 mg/l related to DOC (Dissolved Organic Carbon) related to
Contact time	:	
Degradation	:	= 0 (±) % after 75 day(s)
Result	:	
Deg. product	:	
Method	:	other: Biodegradation under methanogenic conditions
Year	:	
GLP	:	no data
Test substance	:	other TS
Remark	:	The gas production in the test bottles was lower than that in blanks.
Source	:	BUA - TU München Freising
Test condition	:	Temperature: 35 degree C; The digesting slude was collected from a Sewage Works which receives a mixture of domestic and industrial waste water.
Test substance	:	2-Naphthol
Reliability	:	(2) valid with restrictions

(31)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Remark	:	According to the measured log Pow (2.01 - 2.7) a significant bioaccumulation potential is not to be expected.
Source	:	BUA - TU München Freising

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	flow through
Species	:	Micropterus salmoides (Fish, fresh water)
Exposure period	:	7 day(s)
Unit	:	mg/l
LC50	:	= 1.77
Limit test	:	
Analytical monitoring	:	yes
Method	:	other: Embryo-Larval test
Year	:	
GLP	:	no data
Test substance	:	other TS
Remark	:	Survival of normal (non-teratic) organisms was 62 % at 1.59 mg/l. Teratic larvae were observed at frequencies of 3 % to 6 % over an exposure range of 0.02 to 8.51 mg/l. The LC50 value was 6.36 mg/l (95 % Conf. Lim. 5.85 - 6.91 mg/l) at hatching and 1.77 mg/l (95 % Conf. Lim. 1.67 - 4.51) at 4 days post hatching.
Source	:	BUA - TU München Freising
Test condition	:	Exposure was initiated 2 - 4 h post spawning, average hatching time 3 d, and was continued through 4 days posthatching; total exposuretime 7 d; temperature: 20.2 - 23.2 degree C.
Test substance	:	2-Naphthol
Reliability	:	(2) valid with restrictions

(32)

Type	:	static
Species	:	Gadus morrhua (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	> 3
Limit test	:	
Analytical monitoring	:	yes
Method	:	other: Toxic effects on marine embryos
Year	:	
GLP	:	no data
Test substance	:	other TS
Remark	:	The test was done with fish eggs, starting during the first day after fertilization.
Source	:	BUA - TU München Freising
Test condition	:	Temperature: +5 degree C; the stocksolution was prepared with the test substance mixed with filtered seawater.
Test substance	:	2-Naphthol (>98 % pure)
Reliability	:	(2) valid with restrictions

(33)

Type	:	static
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= 3.46
Limit test	:	
Analytical monitoring	:	yes
Method	:	other: Acute Toxicity to fish
Year	:	
GLP	:	no data

Test substance : other TS

Remark : Juvenile; 95 % Conf. Lim. 2.43 - 3.90 mg/l; mean DO-values decreased from 8.5 mg/l at the start of the tests to 6.5 mg/l at 48 hours.
Source : BUA - TU München Freising
Test condition : T: 20 +/- 0.5 degree C; 7.6-liter aquaria covered with aluminium foil were used as test vessels; each aquaria contained 6 l of test solution and 5 fish. 2 aquaria were used for each of the 3 to 4 test concentrations. Test solution was prepared with well water (pH: 7.8; alkalinity and hardness 120 and 140 mg/l as CaCO3). DO changes from a mean of 8.5 mg/l at time 0 to 4.3 mg/l resp. 6.5 mg/l after 48 h.
Test substance : 2-Naphthol
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint

(34)

Type : static
Species : Poecilia reticulata (Fish, fresh water)
Exposure period : 48 hour(s)
Unit : mg/l
LC50 : = 3
Method : other: Acute Toxicity to fish
Year : 1974
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Source : BUA - TU München Freising
Reliability : (4) not assignable
only test result available

(35)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : semistatic
Species : Crangon septemspinosa (Crustacea)
Exposure period : 96 hour(s)
Unit : mg/l
LT : = 2.5
Analytical monitoring : yes
Method : other: Lethality test
Year :
GLP : no
Test substance : other TS

Remark : LT = Lethal treshold
Source : BUA - TU München Freising
Test condition : Stocksolution were prepared either in ethanol or in dimethyl sulfoxide. The test was done in aerated sea water at 10 degree C with the solutions changed at 48 h. Test performed with 3 shrimps only.
Test substance : 2-Naphthol
Reliability : (3) invalid

(36)

Type :
Species : Daphnia magna (Crustacea)

Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	= 3.54
Analytical monitoring	:	yes
Method	:	other: Acute, static toxicity test
Year	:	
GLP	:	no data
Test substance	:	no data
Remark	:	First instar, juvenile; 95 % Conf. Lim. 3.17 - 3.95 mg/l;
Source	:	BUA - TU München Freising
Test condition	:	T: 19.5 - 20.5 degree C; 6 animals per replicate, 4 replicates for each test concentration; test solution was prepared with well water (pH: 7.8; alkalinity and hardness 120 and 140 mg/l as CaCO3)
Test substance	:	2-Naphthol
Reliability	:	(2) valid with restrictions

(34)

Type	:	
Species	:	Daphnia magna (Crustacea)
Exposure period	:	24 hour(s)
Unit	:	mg/l
EC50	:	5 - 10
Method	:	other: DIN 38412 Teil 11
Year	:	1980
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	BUA - TU München Freising
Reliability	:	(4) not assignable only test result available

(29)

Type	:	
Species	:	Gammarus minus (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	= .85
Analytical monitoring	:	yes
Method	:	other: Acute, static toxicity test
Year	:	
GLP	:	no data
Test substance	:	other TS
Remark	:	Adult animals collected from a local stream; 95 % Conf. Lim. 0.7 - 1.03 mg/l;
Source	:	BUA - TU München Freising
Test condition	:	T: 21-24 degree C; covered 100-ml beakers filled with 75 ml test solution were used as test vessels. test solution was prepared with well water (pH: 7.8; alkalinity and hardness 120 and 140 mg/l as CaCO3); 4 replicates of five animals were used for each of the 5 test concentrations.
Test substance	:	2-Naphthol
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

(34)

Type	:	semistatic
Species	:	other aquatic mollusc: Mya arenaria
Exposure period	:	96 hour(s)

Unit	:	mg/l
LT	:	= 17
Analytical monitoring	:	yes
Method	:	other: Lethality test
Year	:	
GLP	:	yes
Test substance	:	other TS
Remark	:	LT = Lethal treshold
Source	:	BUA - TU München Freising
Test condition	:	Stocksolution were prepared either in ethanol or in dimethyl sulfoxide. The test was done in aerated seawater at 10 degree C with the solutions changed at 48 h. 3 clams for each test concentration.
Test substance	:	2-Naphthol
Reliability	:	(3) invalid

(36)

Type	:	
Species	:	other aquatic mollusc: Physa gyrina
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	= 24.7
Analytical monitoring	:	yes
Method	:	other: Acute Toxicity Test
Year	:	
GLP	:	no data
Test substance	:	other TS
Remark	:	95 % Conf. Lim. 22.4 - 27.9 mg/l;
Source	:	BUA - TU München Freising
Test condition	:	T: 19.5 - 20.5 degree C; Test vessels (covered glass Petri dishes) each contained one snail in 60 ml of test solution. test solution was prepared with well water (pH: 7.8; alkalinity and hardness 120 and 140 mg/l as CaCO3); 20 animals were used for each of the 4 to 5 test concentrations.
Test substance	:	2-Naphthol
Reliability	:	(2) valid with restrictions

(34)

Type	:	
Species	:	other: Chironomus tentans
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	= 4.32
Analytical monitoring	:	yes
Method	:	other: acute, static toxicity test
Year	:	
GLP	:	no data
Test substance	:	other TS: 2-naphthol
Remark	:	4th instar larvae; 95% Conf. Lim. 1.15 - 26.3)
Source	:	BUA - TU München Freising
Test condition	:	T: 23-26 degree C, beakers covered with aluminium foil to prevent volatilisation. Test solution was prepared with well water (pH: 7.8; alkalinity and hardness 120 and 140 mg/l as CaCO3); 7 larvae per replicate, 4 replicate per concentration
Reliability	:	(2) valid with restrictions

(34)

Type	:	
Species	:	other: Strongylocentrotus droebachiensis (sea-urchin)
Exposure period	:	96 hour(s)
Unit	:	mg/l
EC50	:	= 1.9
Analytical monitoring	:	yes
Method	:	other: Toxic effects on marine embryos
Year	:	
GLP	:	no data
Test substance	:	other TS
Remark	:	The test was done with eggs, starting during the first day after fertilization.
Source	:	BUA - TU München Freising
Test condition	:	Temperature: 5 degree C; the stocksolution was prepared with the test substance mixed with filtered seawater.
Test substance	:	2-Naphthol (>98 % pure)
Reliability	:	(2) valid with restrictions

(33)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Microcystis aeruginosa (Algae, blue, cyanobacteria)
Endpoint	:	biomass
Exposure period	:	14 day(s)
Unit	:	mg/l
EC20	:	= 20
Limit test	:	
Analytical monitoring	:	no data
Method	:	other: Algal Assay Bottle Test
Year	:	
GLP	:	no data
Test substance	:	other TS
Source	:	BUA - TU München Freising
Test condition	:	Culture flasks were capped with foil to reduce loss of test substance by volatilisation.
Test substance	:	2-Naphthol
Reliability	:	(3) invalid there is no informatio whether the algae were in the exponential growth during the whole exposure time; possible photochemical degradation is not considered

(37)

Species	:	Microcystis aeruginosa (Algae, blue, cyanobacteria)
Endpoint	:	other: Reduction of Photosynthesis
Exposure period	:	4 hour(s)
Unit	:	mg/l
EC20	:	= .75
Limit test	:	
Analytical monitoring	:	no data
Method	:	other: Algal Photosynthesis Bioassay
Year	:	
GLP	:	no data
Test substance	:	other TS
Source	:	BUA - TU München Freising
Test condition	:	Aliquots of the algae culture were distributed to

srew-capped culture tubes. The test substance was the added to in aqueous or acetone solution and the cultures are placed under a bank of fluorescent and incandescent lights (1700 µW/cm² irradiation between 400 and 700 nm) in an environmental chamber at 24 degree C. The cultures are preincubated for 2 h before photosynthesis measurement is begun. After preincubation, cultures are spiked with 0.01 ml of 14C-labelled sodium bicarbonate solution and incubated for another 2 h.

Test substance : 2-Naphthol
Reliability : (2) valid with restrictions

(37)

Species : Nitzschia palea (Algae)
Endpoint : other: Reduction of assimilationrate
Exposure period : 4 hour(s)
Unit : mg/l
EC50 : = 6.3
Limit test :
Analytical monitoring : yes
Method : other: According to Giddings et al. (1983)
Year :
GLP : no data
Test substance : other TS

Remark : 95 % Conf. Lim. 4.62 - 8.3 mg/l
Source : BUA - TU München Freising
Test condition : 7 to 9 concentrations were tested; three replicates at each test concentration;
Test substance : 2-Naphthol
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint

(34)

Species : Selenastrum capricornutum (Algae)
Endpoint : growth rate
Exposure period :
Unit : mg/l
TC : < 1
Limit test :
Analytical monitoring : yes
Method : other: Dynamic bioassay
Year :
GLP : no data
Test substance : other TS

Remark : Threshold concentration
Result : EC50 about 4 mg/l
Source : BUA - TU München Freising
Test condition : Exposure period: until log-growth
Test substance : 2-Naphthol
Reliability : (2) valid with restrictions

(38)

Species : Selenastrum capricornutum (Algae)
Endpoint : growth rate
Exposure period :
Unit : mg/l
TC : < 1
Limit test :
Analytical monitoring : yes

Method : other: Static bioassay
Year :
GLP : no data
Test substance : other TS

Remark : Threshold concentration
Result : EC50 is about 4 mg/l
Source : BUA - TU München Freising
Test condition : Exposure period: until log-growth
Test substance : 2-Naphthol
Reliability : (2) valid with restrictions

(38)

Species : Selenastrum capricornutum (Algae)
Endpoint : other: Reduction of Photosynthesis
Exposure period : 4 hour(s)
Unit : mg/l
EC20 : = 4
Limit test :
Analytical monitoring : no data
Method : other: Algal Photosynthesis Bioassay
Year :
GLP : no data
Test substance : other TS

Source : BUA - TU München Freising
Test condition : Aliquots of the algae culture were distributed to srew-capped culture tubes. The test substance was the added to in aqueous or acetone solution and the cultures are placed under a bank of fluorescent and incandescent lights (1700 µW/cm² irradiation between 400 and 700 nm) in an environmental chamber at 24 degree C. The cultures are preincubated for 2 h before photosynthesis measurement is begun. After preincubation, cultures are spiked with 0.01 ml of 14C-labelled sodium bicarbonate solution and incubated for another 2 h.
Test substance : 2-Naphthol
Reliability : (2) valid with restrictions

(37)

Species : Selenastrum capricornutum (Algae)
Endpoint : other: Reduction of assimilation rate
Exposure period : 4 hour(s)
Unit : mg/l
EC50 : = 18.8
Limit test :
Analytical monitoring : yes
Method : other: According to Giddings et al. (1983)
Year :
GLP : no data
Test substance : other TS

Remark : 95 % Conf. Lim. 15.8 - 22.2 mg/l
Source : BUA - TU München Freising
Test substance : 2-Naphthol
Reliability : (2) valid with restrictions

(34)

Species : other algae: Natural Algal Communicity
Endpoint : other: Reduction of Photosynthesis
Exposure period : 4 hour(s)

Unit : mg/l
EC20 : = 1
Method : other: Algal Photosynthesis Bioassay
Year :
GLP : no data
Test substance : other TS

Source : BUA - TU München Freising
Test condition : Aliquots of the algae culture were distributed to srew-capped culture tubes. The test substance was the added to in aqueous or acetone solution and the cultures are placed under a bank of fluorescent and incandescent lights (1700 µW/cm² irradiation between 400 and 700 nm) in an environmental chamber at 24 degree C. The cultures are preincubated for 2 h before photosynthesis measurement is begun. After preincubation, cultures are spiked with 0.01 ml of 14C-labelled sodium bicarbonate solution and incubated for another 2 h.
Test substance : 2-Naphthol
Reliability : (2) valid with restrictions

(37)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type : aquatic
Species : Aspergillus niger (Fungi)
Exposure period : 48 hour(s)
Unit : mg/l
TC : = 50
Method : other: Agar Cup-Plate method
Year :
GLP : no data
Test substance : other TS

Remark : Threshold concentration (Minimum Inhibition Concentration)
Source : BUA - TU München Freising
Test condition : T: 37 degree C
Test substance : 2-Naphthol
Reliability : (2) valid with restrictions

(39)

Type : aquatic
Species : Staphylococcus aureus (Bacteria)
Exposure period : 48 hour(s)
Unit : mg/l
TC : = 200
Method : other: Streak method
Year :
GLP : no data
Test substance : other TS

Remark : Threshold concentration (Minimum Inhibition Concentration)
Source : BUA - TU München Freising
Test condition : T: 37 degree C
Test substance : 2-Naphthol
Reliability : (2) valid with restrictions

(39)

Type : aquatic

Species : other bacteria: Salmonella typhosa
Exposure period :
Unit : mg/l
TC : = 100
Method : other: Streak method
Year :
GLP : no data
Test substance : no data

Remark : Threshold concentration
Source : BUA - TU München Freising
Test condition : T: 37degree C
Reliability : (2) valid with restrictions
(39)

Type : aquatic
Species : other fungi: Trichophyton gypseum
Exposure period : 48 hour(s)
Unit : mg/l
TC : = 50
Method : other: Agar Cup-Plate method
Year :
GLP : no data
Test substance : no data

Remark : Threshold concentration
Source : BUA - TU München Freising
Test condition : T: 37 degree C
Reliability : (2) valid with restrictions
(39)

Type : aquatic
Species : other fungi: Trichophyton rubrum
Exposure period : 48 hour(s)
Unit : mg/l
TC : = 50
Method : other: Agar Cup-Plate method
Year :
GLP : no data
Test substance : no data

Remark : Threshold concentration
Source : BUA - TU München Freising
Test condition : T: 37 degree C
Reliability : (2) valid with restrictions
(39)

Type : aquatic
Species : anaerobic bact. from a domestic water treatment plant
Exposure period : 24 hour(s)
Unit : mg/l
EC50 : ca. 250
TC : ca. 65
Analytical monitoring : no
Method : other: Fermentation tube test
Year : 1987
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Remark : Threshold concentration
Source : BUA - TU München Freising

Reliability : (4) not assignable
only test result available

(28)

Type : aquatic
Species : anaerobic bact. from a domestic water treatment plant
Exposure period : 24 hour(s)
Unit : mg/l
TC : = 80
Method : other: Fermentation tube test
Year : 1974
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Remark : Threshold concentration
Source : BUA - TU München Freising
Reliability : (4) not assignable
only test result available

(35)

Type : aquatic
Species : anaerobic bact. from a domestic water treatment plant
Exposure period : 24 hour(s)
Unit : mg/l
TC : = 200
Method : other: Fermentation tube test
Year : 1980
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : Threshold concentration
Source : BUA - TU München Freising
Reliability : (4) not assignable
only test result available

(29)

4.5.1 CHRONIC TOXICITY TO FISH

Species : Oncorhynchus mykiss (Fish, fresh water)
Endpoint :
Exposure period : 27 day(s)
Unit : mg/l
NOEC : = .001
Analytical monitoring : yes
Method : other: embryo-larval test
Year :
GLP : no data
Test substance :

Result : Teratic larvae were observed at frequencies of 2 % to 36 % over an exposure range of 0.001 to 0.907 mg/l. The LC50 value was 0.08 mg/l (95 % Conf. Lim. 0.06 - 0.1 mg/l) at hatching and 0.07 mg/l (95 % Conf. Lim. 0.06 - 0.09 mg/l) at 4 days posthatching.
Source : BUA - TU München Freising
Test condition : Flow-through system (flow-rate 200 ml/h, retention time 2.5 h); exposure was initiated 20 min after fertilization, average hatching times were 23 d, and was continued through 4 days posthatching; total exposure time 27 d; 100-150

		eggs/exposure chamber; temperature: 13.3 - 14.2 degree C, dissolved oxygen: 8.6-10.2 mg/l; pH: 7.4 - 8.1; water hardness: 86.8-116.3 mg/l CaCO3; daily analysis of test concentration; 4 - 6 test concentrations, 2 replicates/test
Test substance	:	other: 2-naphthol
Reliability	:	(2) valid with restrictions

(32)

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

Species	:	other avian: Agelaius phoeniceus
Endpoint	:	mortality
Exposure period	:	
Unit	:	mg/kg bw
LC50	:	>= 100
Method	:	other: no data
Year	:	
GLP	:	no data
Test substance	:	other TS
Remark	:	Estimated LD50 based on food consumption data over a 18 h period.
Source	:	BUA - TU München Freising
Test substance	:	2-Naphthol
Reliability	:	(2) valid with restrictions

(40)

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

In Vitro/in vivo : In vitro
Type : Absorption
Species : human
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :

Method : the observed permeability coefficient was obtained by using an in vitro technique
Result : The Human Cutaneous Permeability Coefficient Values (Kp) for 2-naphthol were 0.028 cm/h (observed), and 0.7 cm/h (calculated).
Source : BUA - TU München Freising
Reliability : (4) not assignable
secondary citation

(16)

In Vitro/in vivo : In vitro
Type : Metabolism
Species : guinea pig
Number of animals
Males :
Females :
Doses
Males : 50; 130 nmol/mL
Females :
Vehicle :
Route of administration :
Exposure time : 45 minute(s)
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :
Half-lives : 1st:
2nd:
3rd:
Toxic behaviour :
Deg. product :
Method :
Year : 1993
GLP : no data
Test substance : other TS: 14C-2-naphthol, 51 mCi

Method : 3-8 experiments per dose level and application site (colon and jejunum; luminal and contraluminal, respectively).
Result : 14C-labelled 2-naphthol was added to the luminal or contraluminal fluid bathing the two sides of jejunal or colonic mucosal sheets prepared from male guine pigs. After aerobic incubation for 45 minutes at 37 °C, the fluid compartments and the tissues were analysed for parent drug and metabolites. 2-Naphthol was transformed into its sulphate
and glucuronide. In the jejunum, 2-naphthol was more extensively sulphated than 1-naphthol, whereas in the colon

the metabolite profiles (sulphate:glucuronide ratio) of the two isomers were similar.
When added to the luminal side of jejunal sheets, 2-naphthol was metabolised to about 80% and 3-6 times as much 2-naphthyl sulphate was formed as compared to glucuronide.
In the colon, about 50% of 2-naphthol was metabolized at the low dose level (50 nmol/mL), but only 35% were conjugated at 130 nmol/mL, mainly due to decreased sulphation.

Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
limited documentation (i.e. only mean values reported; recoveries not reported)

(41)

In Vitro/in vivo : In vitro
Type : Metabolism
Species : rat
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :
Method :
Year :
GLP :
Test substance : other TS: 2-naphthol, "highest quality available"

Method : 6-8 animals / group. Assays were performed in duplicate or triplicate samples from each animal. Separate groups of male animals were treated i.p. for four days with either 75 mg phenobarbital/kg in saline, 75 mg pregnenolone-16alpha-carbonitrile/kg suspended in 2% Tween 80 in saline, or 20 mg 2-methylcholanthrene/kg in corn oil. Control animals received either corn oil or saline. All solutions were adninistered in a volume of 5 mL/kg. 24 hrs after the last dose, the rats were anesthetized with urethane and livers were excised, rinsed in ince-cold KCl, and a 25% homogenate in 0.25M sucrose was prepared (containing 10mM Tris-HCl, pH 7.4, and 3 mM 2-mercaptoethanol). After centrifugation at 105,000 g for 65 min, the supernatant was used to quantify sulfotransferase activity by using the colorimetric method of Nose and Lipmann described by Sekura and Jakoby (1979).
Means and standard errors were generated for each group, and the data were analyzed by a one-way or two-way analysis of variance as appropriate. Duncan`s new multiple range test was used to compare the means. Significance was set at $P < 0.05$.
Result : Sulfotransferase activity in male Sprague-Dawley rats for 2-naphthol was 0.641 +/- 0.021 nmol/min/mg protein (mean +/- SD for 15 rats). Sulfation in cotton rats was only 15-30% of that observed in SD rats and was not increased by inducer administration.
Source : BUA - TU München Freising
Reliability : (1) valid without restriction

(42)

In Vitro/in vivo : In vivo
Type : Distribution

Species : mouse
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :
Route of administration : i.p.
Exposure time : 24 hour(s)
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :
Half-lives : 1st:
2nd:
3rd:
Toxic behaviour :
Deg. product :
Method :
Year :
GLP :
Test substance : other TS: 2-naphthol, purity 98%

Method : in this study the pulmonary toxicity of 2-isopropylnaphthalene and its photoproducts was studied.
Test substances: 2-isopropenylnaphthalene, 2-acetonaphtone, 2-naphthol, phthalide, phthalic acid, 2-(2-naphthyl)-2-propanol.
3-5 animals / group.
Result : Concentrations of 2-naphthol in lung, liver and kidney were highest within 1 to 2 hours after i.p. administration of 50 mg/kg, and then rapidly decreased.
The binding of 2-naphthol to lung slices was comparable to that seen in 2-methylnaphthalene and damage of Clara cells was also found.
2-Naphthol caused significant depletion of pulmonary GSH levels (reduced glutathione) at 12 hours after the administration of the compound.
Treatment with 2-naphthol did not affect lipid peroxidation and phospholidpid levels in the lung.
Source : BUA - TU München Freising
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint

(43)

In Vitro/in vivo :
Type :
Species : rat
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :

Result : No significant changes were observed in sulfotransferase activity with age in either male or female rats using 2-naphthol as the substrate.
Source : BUA - TU München Freising
Reliability : (4) not assignable

secondary citation

(44)

In Vitro/in vivo : In vitro
Type : Metabolism
Species : human
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :
Method :
Year :
GLP : no data
Test substance : other TS: 2-naphthol, obtained from Sigma

Result : The activity of the microsomal glucuronyltransferase was measured in 34 fetal and 27 adult human livers with 2-naphthol as substrate. The average enzyme activity was 0.07 +/- 0.07 nmol/min/mg protein in fetal and 7.98 +/- 4.19 nmol/min/mg protein in adult livers.
The activity of the cytosolic sulphotransferase was measured with 2-naphthol as substrate in 30 fetal and 23 adult livers. Mean activity was 0.18 +/- 0.12 nmol/min/mg protein in fetal and 0.63 +/- 0.22 nmol/min/mg protein in adult livers. No relationship was observed between the activity of the glucuronyltransferase and sulfotransferase and gestational age.
Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
livers obtained at laparatomy from patients undergoing cholecystectomy. Anaesthesia may have influenced enzyme activity.
Flag : Critical study for SIDS endpoint

(45)

In Vitro/in vivo : In vivo
Type : Toxicokinetics
Species : human
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :
Route of administration : dermal
Exposure time :
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :
Half-lives : 1st:
2nd:
3rd:
Toxic behaviour :
Deg. product :
Method :
Year : 1972
GLP : no

Test substance : other TS: 2-naphthol, 20% in a "

Method : The subjects studied were patients aged from 18-22 years under treatment for gross acne vulgaris, involving face, neck and trunk in various degrees.
The subjects were free of demonstrable hepatic and renal disease.
The so-called peeling paste contained 20% 2-naphthol, 20% soft soap, 10% precipitated sulphur and 50% soft paraffin.
The paste was applied daily to about 5% of the body surface with a spatula, covered with bandages and left on the skin for approximately 7 hours. The applications were repeated until marked desquamation with inflammation resulted in removal of comedones and suppression of the acne.
24 hours urine was collected during the hospitalization of 10 subjects treated with 7.5 g paste. In addition, blood and urine samples of 4 subjects were taken on one or more days during the treatment period. Venous blood samples were taken 0, 1, 3, 8, 12, and 24 hours after application of the paste.
The free plasma and urine 2-naphthol was extracted on the day of collection.

Result : The 24 hours urinary excretion data showed that there was an average recovery of about 5% of the dose applied to about 5% of the body surface area. Plasma levels of 2-naphthol were significantly lower than the plasma levels of conjugated 2-naphthol. Plasma levels of free 2-naphthol reached a peak level 12 hours after application of the paste. The highest value was approx. 4 ug/mL. Two days after the last application the free 2-naphthol began to dippear from the blood. The plasma levels of conjugated 2-naphthol reached peak level within between 3 and 8 hours after application with max. levels of 21.7 - 23.0 ug/mL. 24 hours after application the mean value was 10.4 ug/mL. In 4 subjects the apparent biological half life of conjugated 2-naphthol varied between extremes of 8 hours and 33 hours.
The cutaneous barriers were found to be easily traversed by 2-naphthol.

Source : BUA - TU München Freising

Reliability : (2) valid with restrictions
Treatment of the skin with a "peeling paste" may have changed the conditions in such a way that percutaneous absorption occurs readily

Flag : Critical study for SIDS endpoint

(46)

In Vitro/in vivo : In vivo
Type : Metabolism
Species : rat
Number of animals
Males :
Females :
Doses
Males : 100 mg/kg per day for 7 days
Females :
Vehicle : other: corn oil
Route of administration : i.p.
Exposure time :
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :
Half-lives : 1st:

2nd:
3rd:

Toxic behaviour :
Deg. product :
Method :
Year :
GLP : no data
Test substance : other TS: 2-naphthol, not specified

Method : 24 hour urine samples were collected after the last dose and the animals were then killed for the determination of the hepatic biochemical parameters.
Result : The administration of 2-naphthol to rats for 7 days had no effect on hepatic microsomal mixed function oxidase-dependent phase-I biotransformation reactions as assessed by the activities of ethylmorphine N-demethylase and aniline 4-hydroxylase. Furthermore, there were no significant changes in either microsomal cytochrome P-450 content or in liver weight. Analysis of urine samples showed that 2-naphthol had no significant effect on the excretion of D-glucaric acid, L-gulonic acid or xylitol. 2-Naphthol significantly stimulated the urinary excretion of conjugated D-glucuronic acid, but had no influence on the urinary exretion of free D-glucuronic acid. It was also not accompanied by an increased excretion of other D-glucuronic acid metabolites.
Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
limited documentation
Flag : Critical study for SIDS endpoint

(47)

In Vitro/in vivo : In vitro
Type : Metabolism
Species : rat
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :

Result : Sulphoconjugation of 2-naphthol was more rapid in seven-week-old male rats than in seven-week-old females. The sulphoconjugation by the supernatants from two-year-old rats did not show significant sex-related differences. Sulphoconjugation activity in the fetus was very low or negligible, and attained nearly half the level of adult female rats in the neonates 2 days after birth.
Source : BUA - TU München Freising
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint

(48) (49)

In Vitro/in vivo : In vivo
Type : Excretion
Species : human
Number of animals
Males :
Females :

Doses
Males :
Females :
Vehicle :

Result : 2-naphthol was found in the urine of a young man after the application of 2-naphthol to his skin for treatment of acne vulgaris. It was estimated that about 3-4 g of the compound was applied to about 20 per cent of the surface area of the patient for 12 hours. 376 mg 2-naphthol were isolated from the complete 48-hour specimen of urine, corresponding to approximately 9.5-12.5 % of the applied dose).
Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
Limited documentation
Flag : Critical study for SIDS endpoint

(50)

In Vitro/in vivo : In vitro
Type : Absorption
Species : human
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :

Method : epidermal membranes were separated from human abdominal skin obtained at autopsy by exposure to ammonia fumes for 30 minutes. Skin samples from one area of one subject were used for each series of experiments. All studies were made at least in duplicate. If necessary each membrane was used for several experiments. Its integrity was examined at the end of each series by repeating the initial experiment and comparimg the fluxes obtained.
Result : The Human Cutaneous Permeability Coefficient Value (Kp) for 2-naphthol in aqueous solution was 0.0279 cm/h. A lag time of 30 minutes was observed with a 0.05% (w/v) aqueous solution.
Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
small number of samples; no reference substance used;
Flag : Critical study for SIDS endpoint

(51)

In Vitro/in vivo : In vitro
Type : Metabolism
Species :
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :

Result : Human liver cytosol catalysed sulphoconjugation of 2-naphthol in the presence of 3-phosphoadenosine 5-phosphosulphate (PAPS), but there were wide

interindividual differences (n=10; mean: 128 +/- 49 pmol/min/mg protein; range: 32-200 pmol/min/mg protein; 75 uM 2-naphthol; pH 7.4)

Source : BUA - TU München Freising
Reliability : (1) valid without restriction

(52)

In Vitro/in vivo : In vitro
Type : Metabolism
Species : other: rat, sheep, cattle, swine
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :

Method : In this experiment, homogenate preparations from fresh livers of cattle, sheep, swine and rats were asayed for microsomal cytochrome P-450 contents, for mixed-function oxidase activities and for a wide array of conjugative activities using numerous xenobiotic substrates. Female catlle, sheep and swine were used and male rats.
Result : Activities of Hepatic Sulfotranferase was as follows (nmol/min/mg protein; mean +/- standard deviation; n= 5-6):
rat: 0.785 +/- 0.066
sheep: 2.090 +/- 0.218
cattle: 2.960 +/- 0.174
swine: 0.095 +/- 0.025
Source : BUA - TU München Freising
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint

(53)

In Vitro/in vivo : In vitro
Type : Metabolism
Species : rat
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :
Method :
Year :
GLP :
Test substance : other TS: 2-naphthol from Merck (Darmstadt, Germany)

Method : Groups of four rats were assigned to each treatment. Each animal was treated by intraperitoneal injection of 0.5 mL of vehicle per 200 g of bw. One group received phenobarbital (80 mg/kg bw) daily for 4 days. Another group received 3-methylcholanthrene in corn oil as a single injection of 80 mg/kg on the first day and these animals were killed on day 5. Animals were sacrificed 24 hr after the last treatment and liver microsomes were prepared. UDGPT activities were measured by photometry for 10 minutes after addition of the test substance. Readings were taken every 20 seconds at 340 nm.

Result : An increased conjugation was observed in liver microsomes from Wistar rats after 3-methylcholanthrene (3-MC) induction, but not after induction with phenobarbital. UDP-glucuronosyltransferase activities after incubation with 0.25 mM 2-naphthol:
controls (oil): 42.9 +/- 0.8 nmoles/min/mg;
after 3-MC: 188.9 +/- 4.0 nmoles/min/mg.
(values represent mean +/- SD of four determinations on pooled microsomes of four animals)
Source : BUA - TU München Freising
Reliability : (1) valid without restriction

(54)

In Vitro/in vivo : In vivo
Type : Metabolism
Species : rat
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :

Result : In vivo, naphthols and methylthio-containing metabolites of naphthalene are formed during enterohepatic circulation of 1,2-dihydro-1-hydroxy-2-S-cysteinylnaphthalene and 1,2-dihydro-1-hydrocy-2-S-(N-acetyl)cysteinyl-naphthalene in a process dependent upon intestinal microflora. The essential role of the intestinal microflora in the formation of naphthols from naphthalene was noted by the authors.
Source : BUA - TU München Freising
Reliability : (1) valid without restriction

(55)

In Vitro/in vivo : In vivo
Type : Absorption
Species : dog
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle : other: ointment (not further specified; in some experiments the ointment contained "soap")
Route of administration : dermal
Exposure time :
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :
Half-lives : 1st:
2nd:
3rd:
Toxic behaviour :
Deg. product :
Method :
Year : 1972
GLP :
Test substance : other TS: 2-naphthol (1, 3, 5, 20 % w/w in ointment)

Method	:	A dog (17 kg) was treated with 30 g of a paste containing 2-naphthol under occlusive conditions. The paste was applied to 414 or 207 cm2 of shaved skin on the back. The same animal was used for several experiments, with intermittent recovery phases of about 4 weeks. Plasma levels of free and conjugated 2-naphthol were determined.
Result	:	Free and conjugated 2-naphthol was found in plasma 5 minutes after application of a paste containing 20% naphthol and soap. The plasma levels increased for approx. 6 hours almost linearly, and reached maximum levels of 27 ug/mL (after treatment of 414 cm2) and 13 ug/mL (extrapolated value; after treatment of 207 cm2). The penetration rate was dependent on the percentage content of 2-naphthol in the paste: 0.5 ug/cm2 per minute (1% naphthol in paste) 1.1 ug/cm2 per minute (3% naphthol in paste), 2,7 ug/cm2 per minute (5% naphthol in paste), and 1.9 ug/cm2 per minute (20% naphthol in paste). Pastes that did not contain soap, released less 2-naphthol: 1.2 ug/cm2 per minute (5% naphthol in paste), and 1.1 ug7cm2 per minute (20% naphthol in paste). Urinary excretion of free and conjugated 2-naphthol was negligible (no quantitative data available).
Source	:	BUA - TU München Freising
Reliability	:	(4) not assignable secondary citation
Flag	:	Critical study for SIDS endpoint

(56)

In Vitro/in vivo	:	In vivo
Type	:	Toxicokinetics
Species	:	dog
Number of animals		
Males	:	
Females	:	
Doses		
Males	:	
Females	:	
Vehicle	:	
Method	:	
Year	:	1972
GLP	:	no
Test substance	:	other TS: 2-naphthol, according to Netherlands Pharmacopeia VI

Method	:	A beagle dog (10 kg) was treated intravenously with 480 mg 2-naphthol by continous infusion over 60 minutes. Plasma levels of free and conjugated 2-naphthol were measured by gas chromatography (detection limit 2 ug/mL). The experiment was performed twice in the same dog. A second dog (17 kg) was treated intravenously with 200 mg 2-naphthol by continous infusion over 107 or 286 minutes. In addition to the determination of plasma levels of free and conjugated 2-naphthol, the amount of free and conjugated 2-naphthol was determined in urine.
Result	:	Maximum plasma levels of free 2-naphthol were detected 60 minutes after infusion (30 ug/mL). During the following 4 hours the plasma levels decreased to 2.5 ug/mL. Plasma elimination half-lives of 0.24 and 3.87 hours were determined for a first, quick elimination phase and a slower phase, respectively.

Conjugated 2-naphthol was at its maximum levels after 60 minutes (60 ug/mL). Thereafter, only a slow decrease was noted, and after 5 hours the values were still around 35 ug/mL (no further time points were examined).
In the second animal, free 2-naphthol levels after 107 minutes were 5 ug/mL, and had decreased to 2 ug/mL after further 7 hours. The maximum level of conjugate was determined in plasma after 2 hours (30 ug/mL) and remained practically constant for further 7 hours. Only after 8.3 days (200 hours) the plasma levels had decreased to detection limits.
Urinary excretion rates for free and conjugated 2-naphthol were approx. 8 and 40 ug/minute, respectively, after 30 minutes and reached maximum levels at 60 minutes (2-naphthol: 60 ug/min; conjugated naphthol: 200 ug/min). During the following 7 hours the urinary excretion rates decreased to 5 ug/mL.
The infusion of 200 mg 2-naphthol for 286 minutes resulted in delayed plasma peak levels and delayed urinary excretion as compared to the infusion over 107 minutes.

Source : BUA - TU München Freising
Reliability : (4) not assignable
secondary citation
Flag : Critical study for SIDS endpoint

(56)

In Vitro/in vivo : In vivo
Type : Toxicokinetics
Species : rat
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :
Route of administration : s.c.
Exposure time :
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :
Half-lives : 1st.:
2nd.:
3rd.:
Toxic behaviour :
Deg. product :
Method :
Year :
GLP :
Test substance : other TS: 2-naphthol, purity not

Method : 3 groups of each 6 male and 6 female Wistar rats (180-220g) were injected subcutanously with 1 mL of a 12.5% solution of 2-naphthol in corn oil for two days (corresponding to 125 mg 2-naphthol / rat). For two further days the rats were administered 0.5 mL (62.5 mg 2-naphthol / rat).
Urine samples were collected for 6 days, starting after the first injection.
Result : The following were detected in urine sampled for 6 days after the last application:
unchanged 2-naphthol (9-13.5% of applied dose),

2-naphthylglucoronide (18-22.5% of applied dose), and
2-naphthyl sulphate (1.6-2% of applied dose).

Source : BUA - TU München Freising
Reliability : (4) not assignable
secondary citation

(57)

In Vitro/in vivo : In vivo
Type : Metabolism
Species : other: cat, swine, rat
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :
Route of administration : i.p.
Exposure time :
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :
Half-lives : 1st:
2nd:
3rd:
Toxic behaviour :
Deg. product :
Method :
Year : 1974
GLP : no
Test substance : other TS: 14C-2-naphthol, purity not stated

Method : cats: 2.5-3.5 kg, sex not specified; number not specified.
swine: males: 16 weeks of age, 20-22 kg; females: 10-15 weeks of age, 12-15 kg; number not given.
rats: females, 190-210 g.
The 8-14C-2-naphthol was administered in each species at a dose of 25 mg/kg.

Result : In cats, 73% of the applied dose was recovered in the urine within 24 hours. The main metabolite was the sulphoconjugate (approx. 98%).
Swine excreted 84% of the applied dose within 24 hours in the urine. The main metabolite was the glucuronide (approx. 94%).
In rats, 86% of the applied dose was recovered in the urine within 24 hours. The main metabolites were the sulphoconjugate (approx. 48%), and the glucuronide (approx. 48%).

Source : BUA - TU München Freising
Reliability : (4) not assignable
secondary citation
Flag : Critical study for SIDS endpoint

(58)

5.1.1 ACUTE ORAL TOXICITY

Type : LD50
Value : = 1320 mg/kg bw
Species : rat
Strain : Wistar

Sex	:	male/female
Number of animals	:	10
Vehicle	:	other: oleum sesami (Ph. Eur. III)
Doses	:	1250; 1600; 2000; 2500 mg/kg bw
Method	:	OECD Guide-line 401 "Acute Oral Toxicity"
Year	:	1986
GLP	:	yes
Test substance	:	other TS: 2-naphthol, purity > 99% (impurity: 0.3% 1-naphthol)
Method	:	5 animals per sex per dose. Fasted animals (food withdrawn 16 hours before application). The test substance was applied as a 25% preparation in sesam oil. Post-observation period: 14 days. Statistics: Probit analysis.
Result	:	LD50 (m/f): 1320 mg/kg bw (95% confidence limits: 728-1560 mg/kg bw). LD50 (m): 1300 mg/kg bw (95% confidence limits: 426-1710 mg/kg bw). LD50 (f): 1340 mg/kg bw (95% confidence limits: 469-1750 mg/kg bw). Mortality: 1250 mg/kg: 2/5 (m), 2/5 (f) 1600 mg/kg: 3/5 (m), 4/5 (f) 2000 mg/kg: 5/5 (m), 5/5 (f) 25ßß mg/kg: 5/5 (m), 4/5 (f) Mortality occurred within 3 days after exposure. Clinical Signs: on day of application: reduced activity, prostrate and lateral positions, irregular breathing, rough coat, closure of eyes. At doses levels >= 1600 mg/kg also tumbling, seizures and reduced reflex activity. Nasal discharge and diarrhoe was observed from day 1 after administration. All surviving animals were free of symptoms on day 5 after exposure at the latest. One female of the 2500 mg/kg group showed reduced body weight gain. At necropsy, vascular injection of the gastro-intestinal tract, inflated stomach, intestinal hemorrhage and urinary bladder filled with brownish liquid were seen. Animals that were killed at the end of the post-observation period were free of pathological changes.
Source	:	BUA - TU München Freising
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

(59)

Type	:	LD50
Value	:	ca. 1500 mg/kg bw
Species	:	rat
Strain	:	no data
Sex	:	no data
Number of animals	:	
Vehicle	:	other: no data
Doses	:	no data
Method	:	
Year	:	1975
GLP	:	no
Test substance	:	other TS: purity not stated

Method : post-exposure observation period: 14 days.
Result : clinical signs: dyspnoe, apathy, prostration, tremors, pallor, diarrhoe, lacrimation (no dose levels specified) findings at necropsy in animals that had died during the study: dilated hearts, general congestion, hemorrhages in forestomach, dark coloured urine.
Source : BUA - TU München Freising
Reliability : (4) not assignable
insufficient detail reported for assessment

(60)

Type : LD50
Value : = 1960 mg/kg bw
Species : rat
Strain :
Sex : male
Number of animals :
Vehicle :
Doses :
Method : other: no data
Year : 1965
GLP : no
Test substance : no data

Source : BUA - TU München Freising
Reliability : (4) not assignable
secondary citation

(61) (62) (63)

Type : LD50
Value : = 2800 mg/kg bw
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method : other: no data
Year : 1971
GLP : no
Test substance : other TS: 2-naphthol, not specified

Source : BUA - TU München Freising
Reliability : (3) invalid
insufficient documentation

(64)

Type : LDLo
Value : = 100 mg/kg bw
Species : mouse
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method : other: no data
Year : 1935
GLP :
Test substance :

Source : BUA - TU München Freising
Reliability : (4) not assignable
secondary citation

(65)

Type : LD50
Value : = 5400 mg/kg bw
Species : rabbit
Strain :
Sex : male
Number of animals :
Vehicle :
Doses :
Method : other: no data
Year : 1965
GLP : no data
Test substance : no data

Source : Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
BUA - TU München Freising
Reliability : (4) not assignable

(66)

Type : LDLo
Value : = 100 mg/kg bw
Species : cat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method : other: no data
Year : 1935
GLP :
Test substance :

Source : BUA - TU München Freising
Reliability : (4) not assignable
secondary citation

(65)

Type : LD50
Value : = 1335 mg/kg bw
Species : guinea pig
Strain :
Sex : male
Number of animals :
Vehicle :
Doses :
Method : other: no data
Year : 1965
GLP : no data
Test substance : no data

Source : BUA - TU München Freising
Reliability : (4) not assignable
secondary citation

(62)

Type	:	LDLo
Value	:	= 3800 mg/kg bw
Species	:	guinea pig
Strain	:	no data
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	other: no data
Year	:	
GLP	:	
Test substance	:	
Source	:	BUA - TU München Freising
Reliability	:	(4) not assignable secondary citation

(67)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Value	:	= 2.2 mg/l
Species	:	rat
Strain	:	Wistar
Sex	:	male/female
Number of animals	:	10
Vehicle	:	other: polyethylene glycol 400 / ethanol (1:1)
Doses	:	0; 0.9; 1.94; 2.5; 5.06 mg 2-naphthol/L (analytical concentrations)
Exposure time	:	4 hour(s)
Method	:	OECD Guide-line 403 "Acute Inhalation Toxicity"
Year	:	1993
GLP	:	yes
Test substance	:	other TS: 2-naphthol, 99.9%
Result	:	clinical signs: irregular breathing, impaired motility, impaired reflexes, blood-stained secretion from nose, encrusted noses, corneal opacities, diarrhoe, and reduced activity were all seen at higher concentrations (the exposure levels at which these signs occurred were not stated). All deaths occurred within 2 days after exposure. In the surviving animals, all clinical signs were fully reversible within 12 days. Reduced body weight gain was noted during the first week after exposure, but was normal at the end of the second week. At necropsy, the animals that had died during the experiment had discoloured and mottled lungs which were foamy and filled with liquid. Animals that survived to the end of the study showed no pathological changes.
Source	:	BUA - TU München Freising
Test condition	:	5 male and 5 female rats (average weights of 192 and 188 g, respectively) were exposed (head-nose) to the 50% aerosol of 2-naphthol in polyethylene glycol 400 / ethanol (1:1). Post-exposure observation period was 14 days. Mean aerodynamic mass diameter: 1.55 um (geometric standard deviation: 2.04)
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

19.01.2006 (68) (69)

Type	:	LC50
Value	:	> .77 mg/l
Species	:	rat
Strain	:	no data
Sex	:	no data
Number of animals	:	6
Vehicle	:	no data
Doses	:	no data
Exposure time	:	1 hour(s)
Method	:	other: no data
Year	:	1973
GLP	:	no
Test substance	:	other TS: 2-naphthol, not specified
Result	:	changes in the structure and function of salivary glands are reported; clinical sign: salivation
Source	:	BUA - TU München Freising
Test condition	:	exposure to dust
Reliability	:	(4) not assignable secondary citation

(70) (71)

Type	:	other: maximal tolerated concentration
Value	:	= .02 mg/l
Species	:	rat
Strain	:	no data
Sex	:	no data
Number of animals	:	
Vehicle	:	
Doses	:	no data
Exposure time	:	unspecified
Method	:	other: no data
Year	:	1973
GLP	:	no data
Test substance	:	no data
Source	:	BUA - TU München Freising
Reliability	:	(3) invalid insufficient detail on conduct of study (eg number of animals, doses not known)

(72)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Value	:	> 10000 mg/kg bw
Species	:	rat
Strain	:	no data
Sex	:	no data
Number of animals	:	
Vehicle	:	no data
Doses	:	no data
Method	:	other: no data
Year	:	1975
GLP	:	no
Test substance	:	other TS: 2-naphthol, not further details
Result	:	no toxic signs noted
Source	:	BUA - TU München Freising

Reliability : (4) not assignable
insufficient detail reported for assessment
Flag : Critical study for SIDS endpoint

(60)

Type : LD50
Value : > 10000 mg/kg bw
Species : rabbit
Strain : no data
Sex : no data
Number of animals :
Vehicle : no data
Doses : no data
Method : other: no data
Year : 1973
GLP : no data
Test substance : other TS: 2-naphthol, no further details

Remark : no further information available
Source : BUA - TU München Freising
Reliability : (4) not assignable
secondary citation; insufficient detail available for assessment.
Flag : Critical study for SIDS endpoint

(71)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type : LD50
Value : = 97500 mg/kg bw
Species : mouse
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Route of admin. : i.p.
Exposure time :
Method : other: no data
Year : 1978
GLP : no data
Test substance : no data

Source : Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
BUA - TU München Freising
Reliability : (3) invalid
value not plausible; secondary citation

(73)

Type : LD50
Value : = 115 mg/kg bw
Species : mouse
Strain : no data
Sex : no data
Number of animals :
Vehicle : no data
Doses : no data
Route of admin. : i.p.
Exposure time :

Method :
Year : 1975
GLP : no
Test substance : other TS: purity not stated

Method : post-exposure observation period: 14 days.
Result : clinical signs: dyspnoe, apathy, prostration, tremor, spastic gait, seizures (not specified at which doses these signs occurred)
Source : BUA - TU München Freising
Reliability : (4) not assignable
insufficient detail reported for assessment

(60)

Type : LDLo
Value : = 2940 mg/kg bw
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Route of admin. : s.c.
Exposure time :
Method : other: no data
Year : 1937
GLP :
Test substance :

Result : clinical signs: sleep, somnolence, general depressed acivity; convulsions.
Source : BUA - TU München Freising
Reliability : (4) not assignable
secondary citation

(74)

Type : LDLo
Value : = 100 mg/kg bw
Species : mouse
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Route of admin. : s.c.
Exposure time :
Method : other: no data
Year : 1909
GLP :
Test substance :

Source : BUA - TU München Freising
Reliability : (4) not assignable
secondary citation

(75)

Type : LDLo
Value : = 3000 mg/kg bw
Species : rabbit
Strain :
Sex :

Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	s.c.
Exposure time	:	
Method	:	other: no data
Year	:	1935
GLP	:	
Test substance	:	
Source	:	BUA - TU München Freising
Reliability	:	(4) not assignable

(65)

Type	:	LDLo
Value	:	= 2670 mg/kg bw
Species	:	guinea pig
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Route of admin.	:	s.c.
Exposure time	:	
Method	:	other: no data
Year	:	1937
GLP	:	
Test substance	:	
Result	:	clinical signs: somnolence, general depressed acivity; convulsions.
Source	:	BUA - TU München Freising
Reliability	:	(4) not assignable secondary citation

(74)

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	500 mg
Exposure	:	Semiocclusive
Exposure time	:	4 hour(s)
Number of animals	:	3
Vehicle	:	physiol. saline
PDII	:	0
Result	:	not irritating
Classification	:	not irritating
Method	:	OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year	:	1986
GLP	:	yes
Test substance	:	other TS: 2-naphthol, purity > 99% (impurity: 0.3% 1-naphthol)
Method	:	The test substance was moistened with 0.3 mL of 0.9 % saline solution.
Result	:	None of the animals showed any sign of irritation (readings at 30-60 minutes, and 24, 48, and 72 hours after application). The Draize scores for erythema and edema were both "0".
Source	:	BUA - TU München Freising

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

(76)

Species	:	rabbit
Concentration	:	500 mg
Exposure	:	no data
Exposure time	:	24 hour(s)
Number of animals	:	6
Vehicle	:	
PDII	:	1.29
Result	:	slightly irritating
Classification	:	
Method	:	
Year	:	1973
GLP	:	no data
Test substance	:	other TS: 2-naphthol, not further specified
Method	:	6 animals each received the pulverized test substance on the intact and abraded back skin. Readings were made after 24 and 72 hours for erythema and edema.
Result	:	Erythema, but no edema was noted. On abraded skin, erythema was still present after 72 hours (score 1.17). The overall score (intact AND abraded skin) was given as 1.29 out of a scale of 8.0. The result is described as "mild effects" in RTECS (2000)
Source	:	BUA - TU München Freising
Reliability	:	(4) not assignable secondary citation
Flag	:	Critical study for SIDS endpoint

(70) (71)

Species	:	rabbit
Concentration	:	
Exposure	:	
Exposure time	:	
Number of animals	:	
Vehicle	:	
PDII	:	
Result	:	irritating
Classification	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	
Source	:	BUA - TU München Freising
Reliability	:	(2) valid with restrictions limited documentation

(77)

Species	:	rabbit
Concentration	:	80 % active substance
Exposure	:	
Exposure time	:	
Number of animals	:	
Vehicle	:	water
PDII	:	
Result	:	slightly irritating
Classification	:	
Method	:	

Year	:	1975
GLP	:	no
Test substance	:	other TS: 2-naphthol, purity not stated
Method	:	A 80% aqueous preparation was applied to the skin of the back for 1, 5 and 15 minutes and for 20 hours. Readings were performed 24 hours after the end of the exposure period.
Result	:	No irritant effects were noted after exposures of 1 and 5 minutes. Slight redness was observed after 15 minutes of exposure, and erythema and edema was seen after an exposure of 20 hours.
Source	:	BUA - TU München Freising
Reliability	:	(4) not assignable insufficient detail reported for assessment

(60)

Species	:	other: QSAR calculation
Concentration	:	
Exposure	:	
Exposure time	:	
Number of animals	:	
Vehicle	:	
PDII	:	
Result	:	
Classification	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	
Result	:	2-Naphthol was predicted non-corrosive in a QSAR model based on principal component analysis.
Source	:	BUA - TU München Freising
Reliability	:	(4) not assignable non-validated QSAR model

19.01.2006 (10)

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	100 mg
Dose	:	
Exposure time	:	24 hour(s)
Comment	:	rinsed after (see exposure time)
Number of animals	:	3
Vehicle	:	none
Result	:	irritating
Classification	:	risk of serious damage to eyes
Method	:	OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year	:	1986
GLP	:	yes
Test substance	:	other TS: 2-naphthol, purity > 99% (impurity: 0.3% 1-naphthol)
Method	:	readings at 1, 24, 48, and 72 hours, and 7 days after administration. At 24 and 72 hours the eyes were also examined under UV light for corneal damage (after instillation of a drop of fluorescein solution).
Result	:	1 - 72 hours after application: conjunctival swelling

(Draize scores 2 and 3), grade 2 conjunctivitis, corneal opacity (grade 1) and irits (grade 1). White discharge. 1 out of 3 animals was free of symptoms after 7 days. The other two animals showed slight to moderate conjunctivitis, one animal had iritis and white discharge. Both animals had corneal opacities with vascularization and conjunctivae were partly detached.

Source : BUA - TU München Freising
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint

(78)

Species : rabbit
Concentration : 100 mg
Dose :
Exposure time :
Comment :
Number of animals :
Vehicle :
Result : moderately irritating
Classification :
Method : other: no data
Year : 1973
GLP : no data
Test substance : other TS: 2-naphthol, not further specified

Source : Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
BUA - TU München Freising
Reliability : (4) not assignable
secondary citation

(71)

Species : rabbit
Concentration :
Dose :
Exposure time :
Comment :
Number of animals :
Vehicle :
Result :
Classification :
Method :
Year :
GLP : no
Test substance : other TS: 2-naphthol, purity not stated

Method : Eyes were removed from sacrificed New Zealand white rabbits and immediately washed in Hanks´ balanced salt solution. Under sterile conditions, the lens organ (lens with epithelium and capsule intact) was removed from the eye using a glass loop after first solubilizing the zonules with alpha-chymotrypsin. The lens organ was incubated at 37°C in RPMI 1640 medium for an initial 24 hours. Then the medium was replaced with 100 mM of the free radical spin trapping agent alpha-phenyl-n-butylnitrone in either fresh RPMI 1640 medium, or the same medium containing 2-naphthol (31.6 - 316 uM; test substance was first dissolved in DMSO; final concentration of DMSO in medium was 5% v/v). Various other naphthalene derivatives (1,4-naphthoquinone, 1-naphthol,

1,2-naphthoquinone) also were tested at equimolar concentrations. At the end of the total 48 hours, an aliquot of the medium was taken for subsequent analysis, and the relative transparency of the lens was determined by viewing a wire grid through the lens. The lens was then homogenized in 6 volumes of hexane, the homogenates centrifuged for 20 minutes at 9000 x g, and the supernatant concentrated to a total volume of 100 uL. The presence of a spin trapped free radical in the organic fraction ws determined using an electron spin resonance spectrometer.
Metabolic activity of the lens organ culture throughout the test period was verified by measuring Na,K-ATP activity according to the method of Post and Senm (Methods of Enzymology, Estabook RW and Pullman ME eds, New York, Academic Press 10, 762 (1967)).

Remark : 1,4-naphthoquinone was cataractogenic in this test system. The result for naphthalene was not consistently reported: "cataractogenic" (in text),and "not cataractogenic" in the results´ table. Discrepancy between reported exposure period (48 hours in methods´ section, 96 hours in abstract).

Result : No lenticular opacities were observed with 2-naphthol in incubations lasting up to 96 hours.

Source : BUA - TU München Freising

Reliability : (3) invalid
Because of problems with solubility even at the lowest concentration, the result may be questionable and further studies using other solvent systems will be necessary to confirm the results according to the authors

(79)

Species : rabbit
Concentration :
Dose :
Exposure time :
Comment :
Number of animals :
Vehicle :
Result : irritating
Classification :
Method :
Year :
GLP :
Test substance :

Source : BUA - TU München Freising

Reliability : (2) valid with restrictions
limited documentation

(77)

Species : rabbit
Concentration : 50 mg
Dose :
Exposure time :
Comment :
Number of animals :
Vehicle :
Result :
Classification : risk of serious damage to eyes
Method :
Year : 1975
GLP : no

Test substance : other TS: 2-naphthol, purity not stated

Result : 1 hour after application slight erythema, slight edema, slight corneal opacity and ocular discharge were noted. After 24 hours erythema and edema were marked, and a slight corneal opacity and slimy appearance of the surface were reported. After 8 days, slight erythema, a marked corneal opacity and vascularization were present.
Source : BUA - TU München Freising
Reliability : (4) not assignable
insufficient detail reported for assessment

(60)

5.3 SENSITIZATION

Type : Guinea pig maximization test
Species : guinea pig
Concentration : 1st: Induction 2 % active substance intracutaneous
2nd: Induction 25 % active substance occlusive epicutaneous
3rd: Challenge 25 % active substance occlusive epicutaneous
Number of animals : 10
Vehicle : other: paraffin (induction), petrolatum (challenge)
Result : sensitizing
Classification : sensitizing
Method : OECD Guide-line 406 "Skin Sensitization"
Year : 1992
GLP : yes
Test substance : other TS: 2-naphthol, purity 99.9%

Result : The treated animals showed no clinical signs of intoxication throughout the study, and the body weight gains were similar to the controls.
All animals of the treatment group showed well defined up to severe erythema and very slight up to slight edema. Additionally, the skin was dry, rough, encrusted, indurated and scabbed. No signs of irritation were observed in the control group 24 and 48 hours after challenge treatment.
Source : BUA - TU München Freising
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint

(80)

Type : Guinea pig maximization test
Species :
Concentration : 1st: Induction 1 % active substance intracutaneous
2nd: Induction 10 % active substance occlusive epicutaneous
3rd: Challenge .1 % active substance open epicutaneous
Number of animals :
Vehicle : other: vaseline (induction), acetone (challenge)
Result : sensitizing
Classification :
Method : OECD Guide-line 406 "Skin Sensitization"
Year : 1985
GLP : no data
Test substance : other TS: 2-naphthol, commercial grade

Method : Guinea pigs were treated intracutaneously with 0.05 mL of a 1% preparation of 2-naphthol in petrolatum and Freund`s Adjuvans. 7 days later, epidermal induction was performed

for 48 hours with a 10% preparation in vaseline. Challenge was performed after 21 days with 20 uL/cm2 solutions in acetone (1 and 0.1%).

Result : 8 out of 8 animals showed positive reactions at 24 hours after challenge with 0.1 or 1% preparations in acetone.
Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
small number of animals; in deviation from OECD 406 the test substance was applied under open conditions for challenge; no reading at 48 hours after challenge.
Flag : Critical study for SIDS endpoint

(81)

Type : Patch-Test
Species : human
Number of animals :
Vehicle : other: olive oil
Result : sensitizing
Classification :
Method : other
Year : 1955
GLP : no
Test substance : other TS: 2-naphthol, purity not stated

Method : The number of patches applied in each patient varied between 1 and 40. No further details.
Result : 2 out of 89 dermatitis patients showed a definite erythema when exposed to a 10% preparation in olive oil.
Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
Poor documentation; no details on methodology
Flag : Critical study for SIDS endpoint

(82)

Type : Patch-Test
Species : human
Number of animals :
Vehicle : other: 1% in petrolatum
Result : not sensitizing
Classification :
Method : other
Year : 1980
GLP : no data
Test substance : other TS: 2-naphthol, recrystallized twice from commercial sample

Method : The tests were performed with Finn Chambers on Scanpor. The application was performed on the back for 2 days. Readings were made according to the ICDRG classification 24 hours after the patches were removed. Patch test concentration was 1% in petrolatum.
Result : Eight patients suffering from pigmented contact dermatitis were patch tested with Sudan I and its several chemical analogues. None of the patients had a positive reaction towards 2-naphthol (tested as 1% in petrolatum). 28 healthy female volunteers, aged 20 and 21, were also tested with these samples as controls. None had a positive reaction.
Source : Hoechst AG Frankfurt/Main
Hoechst AG Frankfurt 80
Hoechst AG Frankfurt/Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
BUA - TU München Freising

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

(83)

Type : Patch-Test
Species : human
Number of animals :
Vehicle : petrolatum
Result : not sensitizing
Classification :
Method :
Year : 1985
GLP : no data
Test substance : other TS: 2-naphthol, not specified

Method : The patch tests were performed with 10 dyes derived from 2-naphthol and with 2-naphthol using Finn chamber on Scanpor tape. They were applied on the back for 48 hours, and the tests read 1h and 24 h after removal according to the ICDRG classification. The patch test concentration was 1% in petrolatum.
Result : Patch tests were performed in a 51-year old man who had been working in a dye factory for 25 years and had noticed itching and pigmentation on the extremities for the past 5 years. The patch tests were performed with 10 dyes derived from 2-naphthol and with 2-naphthol using Finn chamber on Scanpüor tape. They were applied on the back for 48 hr, and the tests read 1h and 24 h after removal according to the ICDRG classification. Positive reactions were found with 2 dyes. 2-Naphthol showed no effects.
Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
limited documentation

(84)

5.4 REPEATED DOSE TOXICITY

Type : Sub-chronic
Species : rat
Sex : male/female
Strain : other: no data
Route of admin. : inhalation
Exposure period : 4 months
Frequency of treatm. : no data
Post exposure period : 1 month
Doses : 0; 0.45; 1.35; 10.1 mg/m³
Control group : yes
NOAEL : = .45 mg/m³
LOAEL : = 1.35 mg/m³
Method : other
Year : 1973
GLP : no
Test substance : other TS: 2-naphthol, not specified

Result : 10.1 mg/m3: lethal for 25% of the animals; surviving animals showed reduced body weight gain (-29.5% after 3 weeks, -47.5% at study end as compared to the controls). In addition, changes in hematology parameters (erythrocyte count, leukocyte count), and histopathologic changes in kidneys and livers.

1.35 mg/m3: No mortality. Effects similar to those in the high-dose group, but less severe. All changes reversible within 1 month after the end of exposure.
0.45 mg/m3: increased N excretion in urine; no histopathological changes.

Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
limited documentation lacking sufficient detail on methodology

(72)

Type : Sub-acute
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : gavage
Exposure period : 28 days
Frequency of treatm. : 7 days/week
Post exposure period : 4 weeks
Doses : 0, 50, 150, 450 mg/kg bw.
Control group : yes
LOAEL : = 50 mg/kg bw
Method : other: similar to OECD Guide-line 407 (1981)
Year : 1989
GLP : yes
Test substance : other TS: 2-naphthol, purity not stated

Method : 5 male and 5 female animals per dose level.
Vehicle: carboxymethyl cellulose (CMC).
The high dose and control groups included 5 additional animals per sex that were sacrificed after the end of the recovery period.
Hematology: according to OECD TG 407
Clinical chemistry/Urinalysis: according to OECD TG 407
Organ examination: no information available

Result : No signs of adverse reactions to treatment were observed in the male rats. Among females, the only sign observed was brown staining of the coat in animals from the high dose group. This sign occurred only during the 4th week of treatment and the first 2 weeks of the recovery period.
There were no treatment-related deaths, and body weight was not affected by the treatment. Food and water consumption was comparable between the groups.
No treatment-related effects were observed at the ophthalmic examinations.
There were no changes in the haematological parameters which could be clearly attributed to treatment with the test substance.
Clinical chemistry parameters for males showed a significant increase in creatinine, sodium and calcium levels, together with a significant decrease in potassium levels in the high dose group at the end of the treatment period. Creatinine levels were significantly decreased in female rats in the high dose group at the end of both the treatment and recovery periods. There were no changes in the urine parameters.
All treated groups showed a slight and not dose-dependent increase in absolute and relative adrenal weights, the significance of this finding is unclear.
There were no treatment-related macroscopic or microscopic abnormalities.

Source	:	BUA - TU München Freising
Reliability	:	(2) valid with restrictions limited documentation (report summary and first 10 pages of report were available for review)
Flag	:	Critical study for SIDS endpoint

(85)

Type	:	Sub-acute
Species	:	rat
Sex	:	female
Strain	:	
Route of admin.	:	gavage
Exposure period	:	10 days
Frequency of treatm.	:	no data
Post exposure period	:	no data
Doses	:	0; 90 mg/kg bw
Control group	:	yes, concurrent no treatment
LOAEL	:	= 90 mg/kg bw
Method	:	
Year	:	1973
GLP	:	no
Test substance	:	other TS: 2-naphthol, purity not stated
Method	:	5 experimental groups; in total 45 animals; weight 100-105 g;
Result	:	The administration of the test substance resulted in a diminished content of nicotinic acid in the blood (-40% vs control) and liver (-30% vs control), and of nictotine-amide coenzymes (-25%) and 1-tryptophan (-75%) in the blood serum. Simultanous administration of 20 mg nicotinic acid per kg bw improved the situation, and 500 IU of vitamin A resulted in normal levels of nicotine-amide coenzyme in the liver.
Source	:	BUA - TU München Freising
Reliability	:	(2) valid with restrictions only some specific parameters investigated; limited documentation.

(86)

Type	:	Sub-acute
Species	:	rat
Sex	:	no data
Strain	:	no data
Route of admin.	:	oral unspecified
Exposure period	:	28 days
Frequency of treatm.	:	continous
Post exposure period	:	no data
Doses	:	no data
Control group	:	no data specified
LOAEL	:	= 10080 mg/kg bw
Method	:	other: no data
Year	:	1973
GLP	:	no
Test substance	:	other TS: 2-naphthol, no further details
Result	:	Weight loss or decreased weight gain. Effects on kidney, ureter, and bladder; changes in bladder weight (no further details).
Source	:	BUA - TU München Freising
Reliability	:	(4) not assignable secondary citation

(71)

Type	:	Sub-chronic
Species	:	rat
Sex	:	no data
Strain	:	no data
Route of admin.	:	oral unspecified
Exposure period	:	35 weeks
Frequency of treatm.	:	intermittent (no details provided)
Post exposure period	:	no data
Doses	:	no data
Control group	:	no data specified
LOAEL	:	= 107 mg/kg bw
Method	:	other: no data
Year	:	1965
GLP	:	no
Test substance	:	

Result	:	Degenerative changes in brain; alteration of reflexes
Source	:	BUA - TU München Freising
Reliability	:	(4) not assignable secondary citation

(87)

Type	:	Sub-chronic
Species	:	rabbit
Sex	:	no data
Strain	:	no data
Route of admin.	:	oral unspecified
Exposure period	:	35 weeks
Frequency of treatm.	:	intermittent (no further details given)
Post exposure period	:	no data
Doses	:	no data
Control group	:	no data specified
LOAEL	:	= 298 mg/kg bw
Method	:	other: no data
Year	:	1965
GLP	:	no
Test substance	:	other TS: 2-naphthol, no further details

Result	:	Liver function tests impaired (no further details available)
Source	:	BUA - TU München Freising
Reliability	:	(4) not assignable secondary citation

(87)

Type	:	Sub-chronic
Species	:	dog
Sex	:	no data
Strain	:	other: no data
Route of admin.	:	s.c.
Exposure period	:	9 months
Frequency of treatm.	:	2/w
Post exposure period	:	no data
Doses	:	25 mg/kg bw
Control group	:	no data specified
LOAEL	:	= 25 mg/kg bw
Method	:	
Year	:	1971
GLP	:	no
Test substance	:	other TS: 2-naphthol, purity not stated

Method	:	3 animals; the test substance was injected as a 7% solution in oil.
Result	:	In the first month of the study kidney function was decreased; after 2-3 months polyuria and hemolysis were observed. Later on albuminuria and microhaematuria was present. It was reported that mainly the kidney tubules were affected resulting in disturbed glomerular function.
Source	:	BUA - TU München Freising
Reliability	:	(2) valid with restrictions limited documentation; small number of animals
Flag	:	Critical study for SIDS endpoint

(88)

Type	:	Sub-chronic
Species	:	other: rat, mice
Sex	:	male/female
Strain	:	
Route of admin.	:	inhalation
Exposure period	:	4 months
Frequency of treatm.	:	no data
Post exposure period	:	not specified
Doses	:	0.1; 1; 10 mg/m3
Control group	:	
LOAEL	:	= 1 mg/m³
Method	:	
Year	:	1973
GLP	:	no
Test substance	:	other TS: 2-naphthol, not specified

Method	:	for the experiments 380 white rats of different ages and sex were used.
Result	:	changes in liver and kidney function. Reduced serum thiol concentration. Transient changes in hematology (not specified). The earliest and most persistent sign was the change in kidney function.
Source	:	BUA - TU München Freising
Reliability	:	(2) valid with restrictions limited documentation lacking detail on methodology

(64)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538
Test concentration	:	no data
Cycotoxic concentr.	:	no data
Metabolic activation	:	with
Result	:	negative
Method	:	other: according to the method described by Ames (1975)
Year	:	1978
GLP	:	no data
Test substance	:	other TS: 2-naphthol from Fluka

Method	:	metabolic activation: rat liver S-9
Source	:	BUA - TU München Freising
Reliability	:	(2) valid with restrictions limited documentation
Flag	:	Critical study for SIDS endpoint

(89)

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA 98, TA 1535, TA 1537, TA 1538, G46, TA1000, C3076, D3052, Escherichia coli WP2 and WP2uvrA-
Test concentration	:	10,000 fold concentration range; no details provided
Cycotoxic concentr.	:	no data
Metabolic activation	:	with and without
Result	:	negative
Method	:	other: Ames-test with the modification described by McMahon, 1979, Cancer Res 39, 682-693
Year	:	1981
GLP	:	no data
Test substance	:	other TS: 2-naphthol, Aldrich Chemical Co.
Remark	:	Ames test utilizing concentration gradient plates (inocula of ten bacterial tester strains were streaked across square agar plates containing a concentration gradient of test compound and mutagenicity was scored by noting the number of tester strains showing mutant colonies over a given concentration range). Each compound was incorporated into four gradient plates to give a tenfold concentration range per plate, thus providing a 10,000-fold concentration range for the test. For metabolic activation, an S9 fraction, derived from the livers of Aroclor 1254 induced rats, was mixed with co-factors and included in an agar overlay on the gradient platres.
Source	:	BUA - TU München Freising
Reliability	:	(2) valid with restrictions summary report; no individual data provided
Flag	:	Critical study for SIDS endpoint

(90)

Type	:	Unscheduled DNA synthesis
System of testing	:	rat hepatocytes
Test concentration	:	0.5 - 1,000 nmoles / mL (8 concentrations)
Cycotoxic concentr.	:	no data
Metabolic activation	:	without
Result	:	negative
Method	:	other: autoradiographic assay, as described by Williams, 1977, Canc Res 37, 1845-51
Year	:	1981
GLP	:	no data
Test substance	:	other TS: 2-naphthol, Aldrich Chemical Co.
Method	:	Primary cultures of adult rat hepatocytes were prepared by in situ perfusion of the liver of 150-170g male Fisher 344 rats as described by Williams, 1977. Yields with 86% to 92% viability were obtained. Exposure period: 5 and 20 hours. 2-AAF and MNNG were used as concurrent positive controls.
Source	:	BUA - TU München Freising
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

(90)

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA 98, TA 100
Test concentration	:	no data
Cycotoxic concentr.	:	no date
Metabolic activation	:	no data
Result	:	negative
Method	:	other: no data
Year	:	

GLP : no data
Test substance : other TS: 2-naphthol, purity not stated

Source : BUA - TU München Freising
Reliability : (4) not assignable
secondary citation

(91) (92)

Type : Bacillus subtilis recombination assay
System of testing : Bacillus subtilis TKJ5211
Test concentration : 50; 500 ug/plate
Cycotoxic concentr. : not cytotoxic
Metabolic activation : with and without
Result : negative
Method : other: spot test
Year : 1977
GLP : no data
Test substance : other TS: 2-naphthol, commercial grade

Method : The constructed strain TKJ5211 shows a particular high sensitivity for His+ reversion and was used in a spot test with 30 selected chemicals.
The test chemicals were dissolved at 5 mg/mL in DMSO.
Metabolic system: S-9 fraction from rat liver homogenate induced by perchlorobiphenyl (PCB).
The dose range of the test chemicals was adjusted so that cell killing "was not severe". usually two doses, 50 ug and 500 ug per plate were used. After 2 days of incubation (with or without a 30 min incubation with S-9) the His+ colonies were counted.
Remark : Methyl methanesulfonate (MMS) and X-rays produced dose-dependent increases in mutant frequencies in this test system.
Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
non-validated test system
Flag : Critical study for SIDS endpoint

(93)

Type : DNA damage and repair assay
System of testing : Bacillus subtilis
Test concentration : no data
Cycotoxic concentr. : no data
Metabolic activation : without
Result : positive
Method : other: no data
Year :
GLP : no data
Test substance : other TS: 2-naphthol, purity not stated

Source : BUA - TU München Freising
Reliability : (4) not assignable
result reported in a table. No details reported on methodology.
Flag : Critical study for SIDS endpoint

(91) (92)

Type : DNA damage and repair assay
System of testing : Escherichia coli AB1157/JC5547, AB1157/JC2921, AB1157/JC2926, AB1157/JC5519, Bacillus subtilis H17/M45, HLL3g/HJ-15
Test concentration : up to maximum amount that was soluble

Cycotoxic concentr. : no data
Metabolic activation : with and without
Result : positive
Method : other
Year : 1982
GLP : no data
Test substance : other TS: 2-naphthol, from Merck-Schuchardt

Method : Each chemical was tested in at least 2 independent experiments with all tester strains and using both the agar-incorporation test and the spot-test method.
S9 rat-liver homogenate from Aroclor-pretreated rats was used for metabolic activation.
The highest concentrations tested were the maximum amounts soluble in dimehtylsulfoxide or distilled water.
Remark : 70 chemicals were tested for their DNA damaging potential.
Result : 2-Naphthol induced DNA repair in Escherichia coli strains, but not in Bacillus subtilis.
Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
non-validated test system
Flag : Critical study for SIDS endpoint

(94)

Type : other: Microsomal degranulation
System of testing : Microsomes of rat liver
Test concentration : 20 ug/ml
Cycotoxic concentr. :
Metabolic activation : no data
Result : negative
Method : other: no data
Year :
GLP : no data
Test substance : other TS: 2-naphthol, purity not stated

Source : BUA - TU München Freising
Reliability : (3) invalid
test system not valid for the evaluation of genetic toxicity

(95)

Type : other: Inhibition of DNA-Synthesis
System of testing : human IMR-90 fibroblasts
Test concentration : 10E-6 M; 10E-9 M
Cycotoxic concentr. : no data
Metabolic activation : no data
Result : negative
Method : other
Year : 1986
GLP : no data
Test substance : other TS: 2-naphthol, purity not stated

Result : The treatment had no effect on DNA synthesis as measured by tritiated thymidine incorporation in synchronized IMR-90 fibroblasts.
Source : BUA - TU München Freising
Reliability : (3) invalid
only very low concentrations tested

(96)

Type : other: SOS-Chromotest
System of testing : Escherichia coli PQ37 (uvrA-) and GC4415 (uvrA-)

Test concentration : no data
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : other: no data
Year :
GLP : no data
Test substance : other TS

Source : Hoechst AG Frankfurt/Main
Hoechst AG Frankfurt 80
Hoechst AG Frankfurt/Main
Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
BUA - TU München Freising
Reliability : (4) not assignable
secondary citation (see source field)

(97)

Type : Ames test
System of testing : Salmonella typhimurium TA100/1535/1537/1538
Test concentration : 1 - 100 µg/Platte
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : other: no data
Year :
GLP : no data
Test substance : no data

Source : Hoechst AG Frankfurt/Main
Clariant GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
BUA - TU München Freising
Reliability : (4) not assignable
report not available

(98)

Type : Ames test
System of testing : Salmonella typhimurium TA1537, TA98, TA1535, TA100
Test concentration : no data
Cycotoxic concentr. : no data
Metabolic activation : with and without
Result : negative
Method : other: spot test and plate incorporation assay
Year : 1978
GLP : no
Test substance : other TS: 2-naphthol, purity not stated

Method : matabolic activation: microsomal fractions from SD rat livers, 37 substances were tested. Vehicle: DMSO.
Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
summary report; no individual data provided for 2-naphthol.
Flag : Critical study for SIDS endpoint

(99) (100)

Type : Ames test
System of testing : Salmonella typhimurium TA98

Test concentration	:	500 uL/ plate of a 2-naphtol solution (50 mg/L), containing nitrite ion (NaNO2, 80 mg/L)
Cycotoxic concentr.	:	no data
Metabolic activation	:	without
Result	:	
Method	:	other: preincubation method (Maron and Ames, Mutat Res 113, 173, 1983)
Year	:	1988
GLP	:	no data
Test substance	:	other TS: 2-naphthol from Kanto Kagaku Co., Japan; best grade available
Remark	:	UV light from 100W high-pressure mercury lamp with maximal energy output at 365 nm, passed through a Pyrex glass filter so as to cut off wavelengths shorter than 300 nm. Each sample was assayed with 4 replicate plates.
Result	:	2-naphthol has been found to exhibit a very strong mutagenicity on UV irradiation at 25 °C in aqueous nitrite solution. The mutagenicity of the ether extract from the solution increased in proportion to the irradiation time. There was evidence that the photochemical oxidation of 2-naphthol to 1,2-naphthoquinone as well as nitration plays an important role in the mutagen formation.
Source	:	BUA - TU München Freising
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

(101)

Type	:	Cytogenetic assay
System of testing	:	Allium cepa
Test concentration	:	0.001 - 10 mmol/L
Cycotoxic concentr.	:	>= 0.5 mmol/L (soft roots)
Metabolic activation	:	without
Result	:	negative
Method	:	other
Year	:	1948
GLP	:	no
Test substance	:	other TS: 2-naphthol, purity not stated
Method	:	A dilution series was prepared, consisting of 13 concentrations. Small Allium Cepa bulbs of the Zittauer variety, which had been grown on tap-water until their roots were about 1 cm in length, were then moved over to these solutions. The roots were observed macroscopically for demonstration of toxicity. Cytological fixations were made on two occasions during the treatment, viz. after an exposure of 4 and 24 hours.
Result	:	About 40 substances containing phenolic OH or (and) NH2 groups were tested as to their activity in inducing chromosome fragmentation. It was found that almost all of them had some activity, although generally a rather low one. 2-naphthol affected mitotic spindle function, however, chromosome fragmentation was extremely rare.
Source	:	BUA - TU München Freising
Reliability	:	(3) invalid Insufficient information on the conduct / conditions of the study; non-validated test system; no controls used;

(102)

Type	:	Ames test
System of testing	:	
Test concentration	:	
Cycotoxic concentr.	:	

Metabolic activation	:	
Result	:	negative
Method	:	
Year	:	
GLP	:	
Test substance	:	

Result	:	2-Naphthol was tested negative by the authors. No further details provided.
Source	:	BUA - TU München Freising
Reliability	:	(4) not assignable

(103)

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA 100, TA 98
Test concentration	:	no data
Cycotoxic concentr.	:	no data
Metabolic activation	:	no data
Result	:	negative
Method	:	other: no data
Year	:	1974
GLP	:	no data
Test substance	:	other TS: 2-naphthol, not further specified

Source	:	BUA - TU München Freising
Reliability	:	(4) not assignable secondary citation

(104)

Type	:	DNA damage and repair assay
System of testing	:	Bacillus subtilis strains HLL3g (wild-type) and HJ-15 (repair deficient)
Test concentration	:	5 mg/mL
Cycotoxic concentr.	:	no data
Metabolic activation	:	without
Result	:	positive
Method	:	other
Year	:	1977
GLP	:	no
Test substance	:	other TS: 2-naphthol, commercial grade

Method	:	A pair of Bacillus subtilis strains was used which differed in their DNA-repair capacity, i.e. the most sensitive mutant HJ-15 and a wild-type strain (HLL3g). HJ-15 is defective in excision repair, recombination capacity and spore repair. DNA repair activity was examined by growth inhibition that was dependent on repairable DNA damage produced by the chemical. The test chemicals were dissolved at 5 mg/mL or saturation in benzene or distilled water. For the repair test, nutrient agar plates were prepared, at whose center a hole of 1 cm diameter was made, and 0.2 mL of agar was sheeted at the bottom. Stationary phase cultures of HLL3g and HJ-15 in nutrient broth were diluted 5-fold with the same medium and streaked on the plate with a glass rod from the edge to the center. 0.1 mL of the test substance was placed in the hole. the plates were incubated at 37 °c overnight, and the growth inhibition zone was measured. The difference in width of the inhibition zone produced with HLL3g and HJ-15 was taken as an indication of the excision and/or recombination repair-dependent DNA damage produced by the chemical. More than 2 mm difference was taken as

positive.
Result : The test chemical slightly induced DNA damage, that was partly repaired in the wild type strain.
Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
limited documentation; non-validated test system
Flag : Critical study for SIDS endpoint

(93)

Type : Cytogenetic assay
System of testing : Vicia faba
Test concentration : no data
Cycotoxic concentr. : no data
Metabolic activation : no data
Result :
Method : other: no data
Year :
GLP : no data
Test substance : other TS: 2-naphthol, no further data

Method : no details on methodology given
Result : 2-naphthol induced chromosome lagging at anaphase, and anaphase bridges in root tip mitoses of Vicia faba.
Source : BUA - TU München Freising
Reliability : (4) not assignable
secondary citation

(105)

Type : other: Inductest
System of testing : E. coli WP2s (lambda)
Test concentration : 1.5 mg/plate
Cycotoxic concentr. : no data
Metabolic activation : with and without
Result : negative
Method : other
Year : 1987
GLP : no data
Test substance : other TS: 2-naphthol, purity not stated

Method : the ability of 30 chemicals to inhibit the release of Lambda phage from lysogenic strains of E. coli was investigated both in the absence and in the presence of metabolic activation sytems (S9-, S14-mix)
Result : 2-naphthol was negative for bacteriophage induction (Inductest) both in the absence and in the presence of metabolic activation (S9-, S14-mix).
Source : BUA - TU München Freising
Reliability : (3) invalid
only one dose level tested; insufficient documentation;

(106)

Type : other: antimutagenic activity
System of testing : Escherichia coli WP2 B/r trp-
Test concentration : no data
Cycotoxic concentr. : not toxic
Metabolic activation : no data
Result :
Method :
Year :
GLP :
Test substance : other TS: 2-naphthol, purest commercial grade

Method	:	Cells were treated with MNNG (5 ug/mL) for 30 minutes at 37 °C and a pre-determined amount of test substance was added to 2 mL of top agar solution.
Result	:	For 2-naphthol, the concentration at which the mutation frequency was reduced to 50% of that of the control was determined as 16 ug/mL. Among the 23 compounds tested, 14 compounds appeared to inhibit the mutagenic effect of MNNG on Escherichia coli. 1- and 2-naphtol were the most potent antimutagens tested. The compounds were not toxic to the test strain at the concentration used, and did not inhibit the expression of Trp+.
Source	:	BUA - TU München Freising
Reliability	:	(2) valid with restrictions limited documentation

(107)

Type	:	Ames test
System of testing	:	Salmonella typhimurium
Test concentration	:	
Cycotoxic concentr.	:	
Metabolic activation	:	
Result	:	negative
Method	:	
Year	:	
GLP	:	
Test substance	:	

Source	:	BUA - TU München Freising
Reliability	:	(4) not assignable

(108)

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA98, TA100, TA1535, TA1537
Test concentration	:	3 umol/plate
Cycotoxic concentr.	:	highly toxic
Metabolic activation	:	with and without
Result	:	negative
Method	:	other: spot test according to Ames, Mut. Res. 31, 347 (1975)
Year	:	1980
GLP	:	no
Test substance	:	other TS: 2-naphthol, > 97%

Source	:	BUA - TU München Freising
Test condition	:	metabolic activation: liver S-9 mix from Aroclor 1254 or methylcholanthrene induced rats; vehicle: ethanol
Reliability	:	(2) valid with restrictions limited documentation (results reported in tabular format)
Flag	:	Critical study for SIDS endpoint

(109)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Micronucleus assay
Species	:	mouse
Sex	:	male
Strain	:	other:BDF1 (C57BL/6 x DBA/2)
Route of admin.	:	gavage
Exposure period	:	2 days

Doses : 62.5, 125, 250, 500, 1000 m/kg bw/day (dose-finding test) 62.5, 125, 250 m/kg bw/day (main test)
Result :
Method : other:OECD Guideline 474 "Mammalian Erythrocyte Micronucleus Test"
Year : 2005
GLP : yes
Test substance : other TS:UENO FINE CHEMICAL INDUSTRY, Lot No, DB1991, Purity:99.5%

Remark : In the dose-finding test, male and female mice (three/sex/group) were given 2-naphthol suspended in 0.5% methylcellulose solution at 62.5, 125, 250, 500 or 1000 mg/kg bw once daily for consecutive two days with 24-hour intervals. Mice were observed for the mortality for 24 hrs after the second administration.

The doses in the main test were determined based on the results of the dose-finding test.
In the main test, male mice were given 2-naphthol suspended in 0.5% methylcellulose solution at 0 (control), 62.5, 125 or 250 mg/kg bw once daily for consecutive two days with 24-hour intervals. Control animals were given 0.5% methylcellulose solution only by gavage.
Dosage volume was 0.1 mL/kg bw in the dose-finding and the main tests.
Positive control animals were once injected intraperitoneally with mitomycin C at 0.5 mg/kg bw. Six male mice at 0, 62.5 and 125 mg/kg bw, and eight male mice at 250 mg/kg bw were used. The animals were killed 24 hours after the second administration, and slides were prepared for bone marrow cells obtained from the femurs. Five specimens per group were examined.

Result : In the dose-finding test (62.5, 125, 250, 500 or 1000 m/kg bw, p.o.), mortalities were in 3/3 (dead mice/mice treated) at 500 and 1000 mg/kg bw in males, and in 1/3 at 250 mg/kg bw and 3/3 at 500 and 1000 mg/kg bw in females. There was no difference between sexes in mortality in the dose-finding test.

In the main test (micronucleus assay), this chemical showed no induction of micronuclei in born marrow polychromatic erythrocytes. The results of micronucleus assay were negative overall.

Dose (mg/kg bw)		0	62.5	125	250
No. of animals examined		5	5	5	5
Frequency of MNPCE (%)	Mean	0.18	0.27	0.22	0.29
	SD	0.08	0.10	0.04	0.09
Range of MNPCE/2000PCE		2-6	3-8	3-5	3-8
Ration of PCE(%)	Mean	57.6	54.6	54.8	48.7
	SD	5.8	2.1	9.8	7.9

Note: MNPCE: Micronucleated polychromatic erythrocyte
PCE : Polychromatic erythrocyte

Reliability : (1) valid without restriction
GLP guideline study
Flag : Critical study for SIDS endpoint
09.02.2006 (110)

Type : Cytogenetic assay
Species : rat
Sex : no data
Strain : no data
Route of admin. : unspecified
Exposure period : no data

Doses	:	no data
Result	:	negative
Method	:	other: no data
Year	:	
GLP	:	no data
Test substance	:	other TS: 2-naphthol, purity not stated
Remark	:	rat bone marrow assay
Source	:	Hoechst AG Frankfurt/Main Hoechst AG Frankfurt 80 Hoechst AG Frankfurt/Main Hoechst AG Frankfurt/Main Clariant GmbH Frankfurt am Main EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) BUA - TU München Freising
Reliability	:	(4) not assignable result reported in a table. No details reported on methodology.
Flag	:	Critical study for SIDS endpoint

(91) (92)

Type	:	
Species	:	other: silk worm
Sex	:	
Strain	:	
Route of admin.	:	other: no data
Exposure period	:	no data
Doses	:	no data
Result	:	negative
Method	:	other: no data
Year	:	
GLP	:	
Test substance	:	other TS: 2-naphthol, purity not stated
Source	:	BUA - TU München Freising
Reliability	:	(4) not assignable result reported in a table. No details reported on methodology.
Flag	:	Critical study for SIDS endpoint

(91) (92)

5.7 CARCINOGENICITY

Species	:	mouse
Sex	:	female
Strain	:	other: different strains
Route of admin.	:	dermal
Exposure period	:	12, 21 weeks
Frequency of treatm.	:	two times per week
Post exposure period	:	not specified
Doses	:	25 ul of a 20 % solution in acetone (12 wk study) or ethanol (21 wk study)
Result	:	negative
Control group	:	other: solvent control and positive control (croton oil)
Method	:	other:
Year	:	1959
GLP	:	no
Test substance	:	other TS: 2-naphthol, purity not stated
Method	:	Initiation with 0.3 % DMBA (75 ug) in acetone or benzene. 36

female mice from four sources, age at study begin: 2-3 months. One week after initiation, 5 mg 2-naphthol (in benzene or acetone) was applied twice per week for 12 or 21 weeks. Mice were examined weekly for tumors.

Remark : Initiation-promotion-study.

Result : 12-week study: 33 of 36 animals survived; 3 % of the animals developed papillomas. None of the animals had skin carcinoma.
21-week study: 21 out of 24 animals survived; none of the animals showed skin papilloma or skin carcinoma.
2-Naphthol had no tumour promoting activity on mouse skin.

Source : BUA - TU München Freising

Reliability : (2) valid with restrictions
study does not meet current standards (small number of animals, limited scope of examinations)

Flag : Critical study for SIDS endpoint

(111)

Species : other: rat, mouse
Sex :
Strain : other: no data
Route of admin. : s.c.
Exposure period : 1 year
Frequency of treatm. : no data
Post exposure period : no data
Doses : no data
Result :
Control group : no data specified
Method : other
Year : 1973
GLP : no
Test substance : other TS: 2-naphthol, not specified

Result : 2 out of 50 treated rats developed malignant tumors within 8 months. 3 out of 100 "mouse embryos" had malignant tumors within 5 months after subcutaneous implantation of beta-naphthol "crystals".
According to the authors, 2-naphthol cannot be considered as a potent carcinogen. In a second publication by the same authors the findings are described as polymorphous-cell sarcomas, and the overall conclusion was that beta-naphthol cannot be regarded even as a weak chemical carcinogen. (no further details available)

Source : BUA - TU München Freising

Reliability : (3) invalid
insufficient detail on conduct of study; no data on controls;

(72) (64)

Species : other: cell transformation in vitro
Sex :
Strain :
Route of admin. :
Exposure period :
Frequency of treatm. :
Post exposure period :
Doses :
Result :
Control group :
Method :
Year : 1997

GLP	:	no data
Test substance	:	other TS: 2-naphthol, > 99%
Method	:	Bovine bronchial epithelial cells were exposed to 0.1 - 1000 uM phenol, catechol, m-cresol, 2-naphthol and 2-naphthyl sulphate. Negative control cultures received media only. After exposure of the chemicals for 7 days, the cultures were fixed, stained and microscopically examined.
Result	:	The proliferative and morphological response of cultured bronchial epithelial cells to several phenolic compounds was determined. Inhibition of growth and transformation to a squamous morphology were observed in response to 2-naphthol exposure (10-100 uM). The responses were observed at subtoxic concentrations and removal of the exposures was followed by renewed proliferation, perhaps by a subpopulation of resistant cells. Of the phenolic compounds tested, catechol was the most active. 2-naphthol had a potency intermediate to catechol and phenol.
Source	:	BUA - TU München Freising
Reliability	:	(2) valid with restrictions non-validated test system
Flag	:	Critical study for SIDS endpoint

(112)

5.8.1 TOXICITY TO FERTILITY

Type	:	One generation study
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	males: for 10 weeks prior to mating, during the mating period and until the day before necropsy (98 days); females: for 2 weeks prior to mating, during mating and gestation and until day 20 of lactation
Frequency of treatm.	:	daily
Premating exposure period		
Male	:	10 weeks
Female	:	2 weeks
Duration of test	:	
No. of generation studies	:	
Doses	:	0; 10; 40; 160 mg/kg bw
Control group	:	yes, concurrent vehicle
NOAEL F1 offspring	:	= 40 mg/kg bw
Method	:	OECD Guide-line 415 "One-generation Reproduction Toxicity Study"
Year	:	2000
GLP	:	yes
Test substance	:	other TS: 2-naphthol, purity 99.6 wt%
Method	:	Vehicle: 0.5% sodium carboxymethylcellulose solution. number of animals: 25 per sex per dose group. Age at initiation: 5 weeks (males), 10 weeks (females). Mating period: max 3 weeks (1:1, until pregnancy or until three weeks had elapsed). Males were sacrificed 1 week after the mating period. Principal organs, pituitary gland, stomach, adrenal glands, testes, epididymides, coagulating glands, seminal vesicles and prostate were isolated and examined. The organs from the control and the high-dose group and all organs with macroscopic abnormalities were processed for

histopathological examinations.
Pregnant females were allowed to deliver spontaneously and were sacrificed on day 21 of lactation together with their offspring. Test substance was applied until the day before sacrifice. At necropsy, all females were examined for abnormalities of the principal organs, the uteri were isolated and the number of implantations counted. In addition, pituitary gland, stomach, adrenal glands, ovaries, cervix and vagina were examined. All organs with macroscopic abnormalities were processed for histopathological examinations.
The parent animals were observed for general condition and for changes in body weight and food consumption as well as reproductive ability including parturition and lactation.
Each litter was examined for number of pups born (live and dead newborns); live newborns were examined for presence of gross anomalies. All dead pups were examined by necropsy.
The offspring were also observed for development up to weaning. On day 4 after birth, the size of each litter was adjusted to 8 pups (four males and four females, in principle). Adjustment was not performed for litters of less than eight pups. Eliminated pups were examined for abnormalities by gross necropsy and fixed in formalin. Live pups were individually weighed on days 0,4,7,14 and 21 after birth, and mean pup weight in each litter was calculated by sex. On day 21 after birth, all live pups were sacrificed and examined for abnormalities by gross necropsy. Organs with abnormalities were fixed in formalin solution.
Statistical analysis: frequency/length of estrous cycle, copulation and fertility indices and frequency of offspring with morphological abnormalities were analyzed by Fisher`s exact probability test. Differences in histopathological findings, the graded data and total numbers of postitives were analyzed by Mann-Whitney`s U-test and one-tailed Fisher`s exact probability test, respectively. Individual data or mean values of each litter were treated as a single sample, and homogeneity of variance of these samples among groups was analyzed using Bartlett`t test. When homogeneity of variance was confirmed, one-way analysis of variance was applied to detect significance between groups. If a significant difference was detected, the Dunnett`s test was applied for multiple comparisons. When variance was not homogenous or zero, the Kruskal-Wallis analysis of ranks was applied, and, if significance was detected, the Dunnett`s test applied for multiple comparisons. Significance levels: p=0.01 and 0.05

Result : Males:
2-Naphthol did not cause death or moribund conditions in the male rats at any dose level.
Transient salivation was observed after dosing in all treatment groups given 2-naphthol. A decrease in locomotor activity was observed after dosing 40 mg/kg or more. The animals in the 40 mg/kg group also showed transient incomplete or complete closure of the eye and nasal discharge. In the group given 160 mg/kg, the animals showed transient lacrimation after dosing.
2-Napththol did not affect body weight gain and food consumption.
At necropsy, thickened forestomach mucosa was observed in the animals of the mid- and high-dose groups.
Histopathological examination revealed squamous hyperplasia of the forestomach in these animals. No micro- or

macroscopic changes were found in the pituitary gland, testes, epididymides, coagulating gland, seminal vesicle and prostate. 10 mg/kg bw caused neither macroscopic nor microscopic changes.

Females:
Neither deaths nor moribund condition were observed in any group. 40 mg/kg caused a transient decrease in locomotor activity and salivation in the early study period. In the animals of the high-dose group, these transient effects were observed after dosing throughout the whole study period. In mid- and high-dose animals nasal discharge, leaning and prone position and reduced activity were also observed after dosing.
While body weight gain was not clearly suppressed, a decrease in food consumption was observed at the beginning of the gestation period in the mid- and high-dose groups.
Food consumption was also decreased after day 4 of lactation in the animals of the high-dose group.
No abnormalities were found at gross necropsy and at microscopic examinations including pituitary gland, stomach, ovaries, uterus, cervix and vagina.

Reproductive Performance:
All females showed normal estrous cycle, and all animals performed fertile copulation. No adverse effect of the test substance was observed on pairing days until conception and number of vaginal estrous during the mating period. Though some females in each group did not become pregnant after copulation, 2-naphthol treatment did not affect fertility index.
Furthermore, no abnormality was found in delivery, on gestation index and gestation length. According to the authors of the study, 160 mg/kg bw could however suppress nursing behaviour, since 2-naphthol was shown to depress activity in dams.

Offspring:
Administration of the test substance did not affect general condition, including behaviour of the offpring. Birth index in the high-dose group was decreased (not statistically significant). The viability index was slightly reduced at day 4 after birth in the high dose group.
There was no effect of 2-naphthol treatment on sex ratio and weaning index.
Decreased body weights were found in the female pups in the high-dose group at day 21 after birth (- 14.5 %). Similar, but less pronounced effects were found in male pups.
No effects on body weight were seen in the low- and mid-dose groups.
One newborn from a dam given 10 mg/kg bw/day was runt. At necropsy, offspring from 1-2 dams in each group, including the control group, showed morphological changes including anomalies and variations. As for external changes, microphthalmia (1 pup), slight subcutaneous hematoma (1 pup) and detachment of the skin (2 pups) were observed in offspring from each one dam in the control, low-dose and high-dose group, respectively. Among these changes, microphthalmia, found in one pup of the control group, was the only change classified as malformation. As for visceral changes, dilatation of the renal pelvis (a variation) was observed in each one pup from dams given 10 or 40 mg/kg bw. Since no significant differences in the incidence of both external and visceral changes and no dose relationships were observed, these effects were judged as chance events.

NOEL for reproductive toxicity, males: 160 mg/kg bw.
NOEL for reproductive toxicity, females and offspring: 40 mg/kg bw. Reduced viability was seen in the offspring at 160 mg/kg bw.
LOEL for systemic toxicity, males: 10 mg/kg bw (salivation)
NOEL for systemic toxicity, females: 10 mg/kg bw (reduced food consumption and decreased locomotor activity at 40 mg/kg bw)

Source : BUA - TU München Freising
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
19.01.2006 (113)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat
Sex :
Strain : Sprague-Dawley
Route of admin. : gavage
Exposure period :
Frequency of treatm. :
Duration of test :
Doses : 0; 10; 40; 160 mg/kg bw
Control group :
NOAEL maternal tox. : = 10 mg/kg bw
NOAEL teratogen. : > 160 - mg/kg bw

Remark : For detailed description of study please cf section 5.8.1 / Toxicity to Fertility
Source : BUA - TU München Freising
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
(113)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

Remark : beta-naphthol was administered to 79 farm workers for treatment of hookworm infection (6g/person for 3 days). The treatment was without any adverse effects in 75 workers, 4 workers had haemolytic reactions resulting in severe anemia, spleen and liver enlargement and haemoglobinuria. 3 out of the 4 workers had had malaria before.
Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
limited documentation; purity of 2-naphthol unknown
Flag : Critical study for SIDS endpoint
(114)

Type of experience : Human

Remark : Analysis in two independent laboratories demonstrated no significant differences in the frequency of chromosome aberrations or micronuclei in lymphocytes from peripheral blood between workers in a chemical factory compared to unexposed control subjects. The workers were exposed to a mixture of chemicals, such as piperazine, low levels of ethylene oxide and formaldehyde, aromatic nitrogen compounds, and other aromatic compounds, such as beta-naphthol.
Source : BUA - TU München Freising
Reliability : (3) invalid
exposure to 2-naphthol not determined; a total of 126 chemicals were handled in the plant producing mainly piperazine; exposure measurements were only reported for piperazine, ethylene oxide and toluene.

(115)

Type of experience : Health records from industry

Result : 303 workers (163 females, 140 males) exposed to 2-naphthol concentrations ranging between 1 and 200 mg/m3 and 126 non-exposed controls were studied. 43% of the workers were exposed for more than 5 years to 2-naphthol.
The results indicated an impairment of kidney function with dysury, nephrosis and inflammation of the urinary bladder. Furthermore, higher incidences of gastric inflammation and chronic hepatitis were observed in the exposed workers as well as impairment of the nervous system, and effects on hematological parameters (reticulocytosis, leucopenia, thrombocytopenia, neutropenia). Contact dermatitis was observed in 21 workers.
Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
limited documentation

(116)

Type of experience : other: oculotoxicity

Result : 2-Napthol may cause effects on retina, lens, iris, and anterior chamber (no details provided).
Source : BUA - TU München Freising
Reliability : (4) not assignable
secondary citation

(117)

Type of experience : Health records from industry

Result : In workers occupationally exposed to 2-naphthol an increased incidence of dermatitis, conjunctivitis, and rhinitis was observed.
Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
limited documentation
Flag : Critical study for SIDS endpoint

(77) (72)

Type of experience : Health records from industry

Result : An increased occupational morbidity with temporary disability and complicated pregnancies with terminations have been reported in female workers employed in the

production of synthetic dyes and intermediates. The authors suggest limitation of exposure, particularly in those dealing with chloro-, nitro- and amino- benzenes.

Source : BUA - TU München Freising
Reliability : (3) invalid
workers exposed to various chemicals; no exposure measurements performed; limited documentation

(118)

Type of experience : Health records from industry

Result : An increased frequency of skin diseases was reported in workers in the aniline dyes industry, particulary in those exposed to aromatic nitroamines.
Source : BUA - TU München Freising
Reliability : (3) invalid
workers exposed to various chemicals; no exposure measurements performed; limited documentation

(119)

Type of experience : Health records from industry

Result : Workers exposed to beta-naphthol had diminished hourly urine volume and urine levels of vitamin C, methyl nicotineamid and 6-pyridoxine levels were decreased. Serum levels of nicotine amide coenzymes were higher as compared to controls. After two months administration of 25 mg nicotinic acid, all changes were reversible.
Source : BUA - TU München Freising
Reliability : (3) invalid
insufficient documentation; co-exposure to other chemicals.

(120)

5.11 ADDITIONAL REMARKS

Type : Cytotoxicity

Result : To establish a bioassay for evaluating immunotoxicological effects, mouse lymphocyte mitogenesis tests of about 255 chemicals were performed. Beta-naphthol had a non-specific inhibitory effect on B cells which was attributed to cytotoxicity (IC50: 7 x 10 e-7 mol/L) and showed no effect on T cell mitogenesis.
Source : BUA - TU München Freising

(121)

Type : Cytotoxicity

Result : The following activities were observed for 2-naphthol on a 10 point scale (0 corresponds to 0-9%, 10 to 100% activity, 305 compounds from various chemical classes were investigated):
Inhibitory effect on cell growth in Ascites sarcome BP8 cells: 8
Inhibition of the oxidative metabolism in hamster brown fat cells: 9
membrane damage of human diploid embryonic lung fibroblasts: 6
inhibition of ciliary activity using chicken embryo trachea

cells: 9

Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
limited documentation;

(122)

Type : other: biomarker

Method : Urine samples were collected from approx. 1000 adults, ranging in age from 20 to 59 years. These adults were selected from a relatively broad spectrum of the U.S. population reflecting both sexes and different age groups, races/ethnicities, urban/rural residences, and regions of the country.

Result : 2-Naphthol was found in 81% of adults living in the United States. The 95th percentile concentration for 2-naphthol was 30 ug/L (18 micrograms per gram creatinine).

Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
limited documentation
Flag : Critical study for SIDS endpoint

(123)

Type : other: biomarker for PAH exposure

Remark : Shipyard workers handling coal-tar or other PAH-related materials were excluded from the study. Spot urine samples were collected from the subjects and kept at -20 °C until analysed. Analytical method: HPLC. Limit of detection: 0.13 ng/mL.
A questionnaire was used to establish gross aspects of lifestyle, ie age, smoking, occupation, and food intake. Statistics: Student`s t-test. Correlation coefficients were calculated between creatinine-adjusted urinary concentrations, with variables related to smoking habit and oral PAH intake, and the statistical significance of coefficients was tested.

Result : A study was undertaken to investigate the distribution pattern of urinary 2-naphthol concentrations in male Koreans with no or low occupational exposure to polycyclic aromatic hydrocarbons (PAHs).
The arithmetic (geometric) means of urinary 2-naphthol concentrations for 129 Korean university students, expressed as micromoles per mole of creatinine were 3.12 (2.22) for all, for non-smokers 1.78 (1.30) and for smokers 4.36 (3.62), respectively. The 95th percentile was 8.29 for all. Among 163 Korean shipyard workers the arithmetic (geometric) means of urinary 2-naphthol concentrations were 4.37 (2.62) for all, 2.46 (1.16) for non-smokers, and 5.60 (4.44) for smokers, respectively. The 95 percentile was 12.06 (for all).
Mean urinary 2-naphthol concentrations differed significantly between non-smokers and smokers both in students and in shipyard workers. Urinary 2-naphthol concentration in smokers was in significant correlation with duration of smoking, with daily amount smoked, with the number of cigarettes moked on the day of sampling, and with the number of cigarettes smoked on the day before sampling. None of the food-related factors (ie intake or frequency of eating charbroiled meat) was significantly correlated with urinary 2-naphthol concentrations.

The authors concluded that urinary 2-naphthol concentrations were a sensitive marker for low-level inhalation of polycyclic aromatic hydrocarbons (PAHs).

Source : BUA - TU München Freising
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint

(124)

Type : other: biomarker for PAH exposure

Method : A questionnaire was used in order to investigate the lifestyles. Urinary naphthols were analyzed by GC/MS/SIM. DNA from blood samples was analyzed for genetic polymorphism of cytochrom P450A1, CYP2E1, glutathione transferase M1 (GSTM1) and N-acetyltransferase (NAT2) by polymerase chain reaction.

Result : In this study, the effects of lifestyle and genetic differences on urinary naphthol levels were investigated in 119 male Japanese workers.
7-fold higher urinary 2-naphthol levels were observed among smokers than non-smokers ($p < 0.001$). Urinary naphthol levels were also related to number of cigarettes smoked and concentrations of urinary cotinine, while not to consumption of food, e.g. meat, fish, etc.
Higher concentrations of urinary naphthols were observed in the c1/c2 or c2/c2 type of CYP2E1 (RsaI genetic polymorphism) than the c1/c1 type and the deficient type of GSTM1 than the normal type ($p <= 0.05$).

Source : BUA - TU München Freising
Reliability : (4) not assignable

(125) (126)

Type : other: biomarker for PAH exposure

Result : The study was undertaken to determine the effects of occupation, lifestyle and the genetic polymorphisms on the concentrations of urinary 1-hydroxypyrene and 2-naphthol among Korean coke oven workers and university students. The study subjects included 90 coke oven workers and 128 university students. Urinary 2-naphthol concentrations were higher in coke oven workers than in students and correlated significantly with work area. Urinary 2-naphthol concentrations increased with an increase in the level of cigarette smoking in students. Urinary 2-naphthol concentrations were higher in coke oven workers with the c1/c2 or c2/c2 genotype of CYP2E1 than in those with the c1/c1 genotype. Urinary 2-naphthol concentrations were higher in GSTM1-null workers than in GSTM1-positive workers. CYP2E1 and GSTM1 were significant determinants for urinary 2-naphthol concentrations in coke oven workers and GSTM1 and smoking were prognosticators among university students.

Source : BUA - TU München Freising
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint

(127)

Type : other: biomarker for PAH exposure

Result : Concentrations of 2-naphthol in urine of coke plant workers were dependent on work area and were highest in distillation departments (mean 630 umol/mol creatinine; ranging up to

1931 umol/mol creatinine; n=29). No statistically significant differences were identified between smokers and non-smokers.

Source : BUA - TU München Freising
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint

(128)

Type : other: cataract formation

Remark : Male C57CL/6 and DBA/2 mice were exposed to 56, 100, 177 or 562 mg/kg bw via the intraperitoneal route (6 animals per group; vehicle: corn oil). At doses of 177 mg/kg bw or above, all animals died within 1.5 hours after administration. One out of 6 animals treated with 177 mg/kg bw showed cataract formation. Animals exposed to 56 or 100 mg/kg bw developped no pathological changes of the eyes.
Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
small number of animals; limited documentation

(129)

Type : other: estrogenicity

Result : 2-Naphthol was shown to interact with the estrogen receptor in rats in a competitive binding assay.
Source : BUA - TU München Freising
Reliability : (4) not assignable
secondary citation

(130)

Type : other: estrogenicity

Result : 2-naphthol (1 uM) showed no agonistic or antagonistic effect on the human progesterone receptor (hPR) activity in yeast (p-nonylphenol, 4-tert-octylphenol and pentachlorophenol had a distinct antagonistic activity in this test system).
Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
non-validated in vitro test system

(131)

Type : other: methaemoglobin formation

Result : In venous blood samples obtained from healthy donors, 2-naphthol caused a modest increase in methaemoglobin, the increase being slightly greater in the absence of glucose (12 vs 8% of the total haemoglobin; controls: 1-2%). 2-Naphthol, present in twice the concentration of GSH, had no discernible effect on the rate of GSH disappearance.
Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
limited documentation

(132)

Type : other: naphthols in cord blood

Method : Analytical method: HPLC. Limit of detection: no data. Statistics: chi-square t-test.
Result : In Ibadan/Nigeria, cord blood samples were collected at delivery and their sera were analysed for naphthols and

aflatoxins. Naphthols were detected in 42 out of 609 serum samples (6.9%; 1-naphthol in 15 samples, 2-naphthol in 21 samples and both naphthols in 6 samples) and aflatoxins in 91 out of 625 samples (14.6%). No correlation was found between the presence of either compound and birthweight (mean birthweight of babies with naphthols in their cord blood: 2.65 (+/- 1.02) kg; mean birthweight of babies without: 2.77 (+/- 0.9) kg. Reported exposure to naphthalene-containing compounds was not related to detection of serum naphthol.
Concentrations of naphthols in serum ranged from 3 to 29026 ug/L (geometric mean concentration 521 ug/L) (no further details in publication).

Source : BUA - TU München Freising
Reliability : (2) valid with restrictions
limited documentation

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