Organisation de Coopération et de Développement Économiques
Organisation for Economic Co-operation and Development

27-Feb-2012

English - Or. English

ENVIRONMENT DIRECTORATE
JOINT MEETING OF THE CHEMICALS COMMITTEE AND THE WORKING PARTY ON CHEMICALS, PESTICIDES AND BIOTECHNOLOGY

Cancels & replaces the same document of 10 February 2012

SIDS Initial Assessment Profiles agreed in the course of the OECD HPV Chemicals Programme from 1993 to 2011

Series on Testing & Assessment
No. 166

The complete document is available in pdf format only.

JT03316623

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ENV/JM/MONO(2012)4/PART1
Unclassified

English - Or. English

OECD Environment, Health and Safety Publications

Series on Testing and Assessment

No. 166

SIDS Initial Assessment Profiles agreed in the course of the OECD HPV Chemicals Programme from 1993-2011

IOMC INTER-ORGANIZATION PROGRAMME FOR THE SOUND MANAGEMENT OF CHEMICALS
A cooperative agreement among FAO, ILO, UNDP, UNEP, UNIDO, UNITAR, WHO, World Bank and OECD

Environment Directorate

ORGANISATION FOR ECONOMIC COOPERATION AND DEVELOPMENT

Paris 2012

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This publication was developed in the IOMC context. The contents do not necessarily reflect the views or stated policies of individual IOMC Participating Organizations.

The Inter-Organisation Programme for the Sound Management of Chemicals (IOMC) was established in 1995 following recommendations made by the 1992 UN Conference on Environment and Development to strengthen co-operation and increase international co-ordination in the field of chemical safety. The Participating Organisations are FAO, ILO, UNDP, UNEP, UNIDO, UNITAR, WHO, World Bank and OECD. The purpose of the IOMC is to promote co-ordination of the policies and activities pursued by the Participating Organisations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

This publication is available electronically, at no charge.

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FOREWORD

OECD works with member countries and other stakeholders to cooperatively assess the hazards of industrial chemicals to generate OECD-agreed assessments that are available to the public and that can be used for priority setting, risk assessment and other activities within national or regional programmes. Further, this cooperative work allows member countries and the chemical industry to share the burden of evaluating chemicals and avoid duplication, which in turn increases efficiencies, decreases costs and minimizes the need for animal testing.

This document presents a collection of SIDS Initial Assessment Profiles (SIAP) presenting hazard conclusions for human health and for the environment for chemicals assessed in the OECD HPV Chemicals Programme between 1993 (1st SIDS Initial Assessment Meeting) and 2011 (32nd SIDS Initial Assessment Meeting).

Each SIAP, together with the full evaluation report once finalised, can be retrieved in the OECD Existing Chemicals database (www.oecd.org/env/existingchemicals/data).

The collection of SIAPs has been divided in six parts, following a chronological order, to keep individual parts to a manageable size. For each part of the document, the corresponding SIDS Initial Assessment Meeting (SIAM) number and the year of the meeting have been indicated below.

		Year
PART 1	SIAM 1 to SIAM 5	1993-1996
PART 2	SIAM 6 to SIAM 10	1997-2000
PART 3	SIAM 11 to SIAM 15	2000-2002
PART 4	SIAM 16 to SIAM 20	2003-2005
PART 5	SIAM 21 to SIAM 25	2005-2007
PART 6	SIAM 26 to SIAM 32	2008-2011

The 32nd SIDS Initial Assessment Meeting was the last one under the OECD HPV Chemicals Assessment Programme before launching the OECD Cooperative Chemicals Assessment Programme (www.oecd.org/env/hazard).

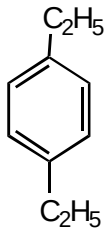
This document is published under the responsibility of the Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology.

List of chemicals assessed at the 1st SIDS Initial Assessment Meeting

To access information relevant to the assessment of individual chemicals, the reader is referred to the OECD Existing Chemical database (http://www.oecd.org/env/existingchemicals/data). No SIDS Initial Assessment Profile was published for individual chemicals at the 1st SIDS Initial Assessment Meeting in 1993, but the entire chemical hazard assessment.

CAS number	Chemical Name
59676	Nicotinic acid
70553	p-Toluenesulfonamide
75912	Hydroperoxide, tert-butyl-
77996	1,3-Propanediol, 2-ethyl-2-(hydroxymethyl)-
79925	Camphene
99092	Aniline, 3-nitro-
107017	2-Butene
126307	1,3-Propanediol, 2,2-dimethyl-
126589	Dipentaerythritol
128392	Phenol, 2,6-bis(1,1-dimethylethyl)-
147148	Copper, phthalocyaninato-
156434	Aniline, 4-ethoxy-
504609	1,3-Pentadiene
536903	Aniline, 3-methoxy-
584032	1,2-Butylene glycol
693232	Dodecanedioic acid
2402791	Pyridine, 2,3,5,6-tetrachloro-
2431507	1-Butene, 2,3,4-trichloro-
3209221	Benzene, 1,2-dichloro-3-nitro-
25265774	Propanoic acid, 2-methyl-, monoester with 2,2,4-trimethyl-1,3-pentanediol
29171208	Dehydrolinalool
29590429	Isooctyl acrylate
6419198	Phosphonic acid, [nitrilotris(methylene)]tris-

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	105-05-5
Chemical Name	Benezene, 1,4-diethyl-
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

It is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Exposure

1,4-Diethylbenzene is a volatile liquid. Its production volume is ca. 1,300 tonnes/year in 1990 - 1992 in Japan and 1,200 tonnes/year were exported to the USA. This chemical is used as a solvent in closed systems. This chemical is stable in neutral, acidic or alkaline solution, and is considered to be “not readily biodegradable” (OECD TG 301C; 0 % by BOD; 0-2 % by GC after 28 days). Experimental BCF values (OECD TG 305) of the chemical are 320 – 629 in carp after 6 weeks.

PECs have been calculated based on a fugacity level III model considering its physico-chemical properties (e.g. molecular weight, water solubility, vapour pressure and partition coefficient). The estimated environmental concentrations were 1.5×10^{-8} mg/l (air), 4.9×10^{-6} mg/l (water), 5.4×10^{-4} mg/kg (soil), 4.6×10^{-3} mg/kg (sediment).

No monitoring data at the work place or the environment have been reported. The chemical is used in closed systems, and no data for consumer use are available. Based on the physico-chemical properties, the total exposed dose indirectly through the environment was estimated to be 8.8×10^{-4} mg/man/day. Also, the daily intake through drinking water is estimated to be 9.7×10^{-6} mg/man/day and through fish is calculated to be 5.7×10^{-4} mg/man/day.

Environment

For the environment, various NOEC and LC_{50} values were gained from test results; 96 h LC_{50} = 1.8 mg/l (acute fish); 24 h EC_{50} = 32 mg/l (acute daphnia); 72 h EC_{50} = 29 mg/l (algae); 21 d NOEC = 0.93 mg/l (long-term daphnia reproduction). As the lowest chronic toxicity result, the 21 d-NOEC (reproduction) for *Daphnia magna* (0.93 mg/l) were adopted. As assessment factor of 100 is applied. Thus the PNEC of 1,4-diethylbenzene is 0.0093 mg/l. Since the PEC is lower than the PNEC, the environmental risk is presumed to be low.

Human Health

The chemical showed no genotoxic effects in bacteria and chromosomal aberration test *in vitro*.

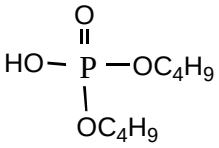
In a combined repeat dose and reproductive/developmental toxicity screening test (OECD TG 422), increases of liver and kidney weights were observed at the dose level of 750 mg/kg/day and 150 mg/kg/day. In relation to the increase of liver weights, increases of incidence of brown colored livers and enlargement of the livers were observed at the highest dose (750 mg/kg/day) with histopathological findings of swelling of liver cells. For reproductive/developmental toxicity end-points, there were no effects observed concerning mating, fertility and oestrus cycle and also for dams during the pregnancy and lactation period. Therefore, the NOEL was 30 mg/kg/day for repeated dose toxicity and 750 mg/kg/day for reproductive toxicity.
The total exposure dose indirectly through the environment was estimated to be 8.8×10^{-4} mg/man/day. Also, the daily intake through drinking water is estimated as 9.7×10^{-6} mg/man/day and through fish is calculated as 5.7×10^{-4} mg/man/day. For human health, the margins of safety by indirect exposure from fish or drinking water are very large. Therefore, health risk is presumed to be low.

In conclusion, no further testing is needed at present considering its toxicity and exposure levels.

NATURE OF FURTHER WORK RECOMMENDED

This chemical is not a candidate for further work because all SIDS endpoints are sufficient.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	107-66-4
Chemical Name	Dibutyl phosphate
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

It is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Dibutyl phosphate is stable liquid and the production volume is ca. 6 tonnes/year in 1990 – 1993 in Japan and 150 - 250 tones/year in 1990 in Germany. This chemical is used as a catalyst for cross-linking in the paint industry. This chemical is stable in neutral, acidic or alkaline solution, and is considered as “inherently biodegradable”. The life time may be relatively long in the environment.

PECs have been calculated based on several models considering its physico-chemical properties (e.g. molecular weight, water solubility, vapour pressure and partition coefficient). The estimated concentrations were 2.4×10^{-14} mg/l (air), 2.5×10^{-7} mg/l (water), 1.9×10^{-6} mg/kg (soil), 1.5×10^{-6} mg/kg (sediment). PEC_{global} was also calculated as 2.5×10^{-7} mg/l, based on a default scenario.

For the environment, various NOEC and LC_{50} values were gained from test results; LC_{50} = 110 - 130 mg/l (acute fish); EC_{50} = 210 mg/l (acute daphnia); EC_{50} = 92 mg/l (acute algae); NOEC = 66 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to be slightly toxic to fish. From the lowest chronic toxicity data to daphnia (21 d-NOEC of 66 mg/l, applying an assessment factor of 100 a PNEC of 0.66 mg/l can be estimated. Since the PEC is lower than the PNEC, the environmental risk is presumably low.

No monitoring data at work place and environment have been reported. The chemical is produced in closed system, and no data for consumer use are available. Based on the physico-chemical properties, the total exposed dose indirectly through the environment was estimated as 3.1×10^{-6} mg/man/day. Also, the daily intake through drinking water is estimated as 5.1×10^{-7} mg/kg/day and through fish is calculated as 3.7×10^{-8} mg/kg/day. No data on occupational exposure are available.

The chemical showed no genotoxic effects in bacteria and chromosomal aberration test *in vitro*.

In a combined repeat dose and reproductive/developmental toxicity screening test, main toxic effects on stomach, bladder and organs related to excretion routes were observed in parental rats. Hepato-toxic effects such as hepatocyte swelled and liver weight increased were also observed. From the view point of reproductive/developmental end-points, there was not any significant effect on fertility or reproductive performance in parental rats. Only a tendency of the decrease in number of live pups was seen at the highest dose (1000 mg/kg/day). The NOEL was 30 mg/kg/day for repeated dose toxicity and 300 mg/kg/day for reproductive toxicity.

The total exposed dose indirectly through the environment was estimated as 3.1×10^{-6} mg/man/day. Also, the daily intake through drinking water is estimated as 5.1×10^{-7} mg/kg/day and through fish is calculated as 3.7×10^{-8} mg/kg/day. For human health, margins of safety by indirect exposure from fish or drinking water are very large. Therefore, the health risk is presumably low.

In conclusion, no further testing is needed at present considering its toxicity and exposure levels.

NATURE OF FURTHER WORK RECOMMENDED

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	24800-44-0
Chemical Name	Tripropylene glycol
Structural Formula	$HO[CH(CH_3)CH_2O]_3H$

CONCLUSIONS AND RECOMMENDATIONS

It is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Trypropylene glycol is a stable liquid with a production volume of ca. 600 tonnes/year in 1990 - 1993 in Japan. This chemical is used as an intermediate for resins in closed systems. It is stable in neutral and acidic solutions, and is considered to be "not readily biodegradable".

PECs have been calculated based on several models considering its physico-chemical properties (e.g. molecular weight, water solubility, vapour pressure and partition coefficient). The estimated concentrations were 9.7×10^{-11} mg/l (air), 8.3×10^{-6} mg/l (water), 3.0×10^{-5} mg/kg (soil), 5.0×10^{-5} mg/kg (sediment).

For the environment, various NOEC and LC_{50} values were gained from test results; LC_{50} = > 1,000 mg/l (acute fish); EC_{50} = > 1,000 mg/l (acute daphnia); EC_{50} = > 1,000 mg/l (acute algae); NOEC = > 1,000 mg/l (long-term daphnia reproduction). Therefore, the chemical does not have any remarkable ecotoxicity. Based on these values and considering the test duration the PNEC for aquatic organisms has been calculated as more than 10 mg/l.

The chemical does not have any remarkable ecotoxicity and its PEC/PNEC ratio is less than 1. Therefore, it is considered to be of low risk for the environment.

No monitoring data at work place have been available. Since the chemical is used as an intermediate in a closed system no data for consumer use are available.

Based on the physico-chemical properties, the level exposed indirectly through the environment was estimated as 5.9×10^{-5} mg/man/day. Also, the daily intake through drinking water is estimated as 2.8×10^{-7} mg/kg/day and through fish is calculated as 2.1×10^{-8} mg/kg/day. No data on occupational exposure are available. Neither monitoring data at work place nor data on consumer exposure have been reported.

The chemical showed no genotoxic effects in bacteria and chromosomal aberration test *in vitro*.

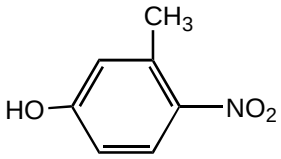
In a combined repeat dose and reproductive/developmental toxicity screening test, only salivation was observed at the highest dose (1000 mg/kg/day). Also, increase in liver and kidney weights were observed in parental animals at that dose. From the view point of reproductive/developmental end-points, there were no effects observed related to mating, fertility and oestrus cycle and also for dams during the pregnancy and lactation period and for pups after their birth. Therefore, NOEL was 200 mg/kg/day for repeated dose toxicity as well as more than 1000 mg/kg/day for reproductive toxicity.

For human health, NOEL was estimated as 200 mg/kg/day and 1000 mg/kg/day for repeated dose and reproductive toxicity, respectively. The total exposed dose indirectly through the environment was estimated as 5.9×10^{-8} mg/man/day. Also, the daily intake through drinking water is estimated as 2.8×10^{-7} mg/kg/day and through fish is calculated as 2.1×10^{-8} mg/kg/day. For human health, margins of safety by indirect exposure from fish or drinking water are very large. Therefore, health risk is presumably low.

In conclusion, no further testing is needed at present considering its toxicity and exposure levels.

NATURE OF FURTHER WORK RECOMMENDED

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	2581-34-2
Chemical Name	Phenol, 3-methyl-4-nitro-
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

Potential risk to man is identified due to genotoxicity and thus presumed carcinogenicity, but measures currently in place reduce risks such that the chemical is of low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

3-Methyl-4-nitrophenol is a stable solid, and the production volume was 3,300 tonnes/year for 1990 - 1993 in Japan. The substance is used as an intermediate for the synthesis of pesticides. Based on an international information gathering activity on exposure, 3-methyl-4-nitrophenol has been produced in two OECD Member countries, i.e. Japan and Denmark. In Japan, the chemical is manufactured and processed in a closed system, i.e. the product itself and all reagents and solvents for its synthesis are handled in perfectly closed tubes and vessels. The synthesis is operated within the same plant. At the work place, protective clothing, gloves and goggles are used. No consumer uses are known. Monitoring data in the general environment in Japan (surface water and sediments) are available, but the substance was not detected in 1984. Regarding the Japanese global situation, the predicted worst case concentration in surface water is 1.7×10^{-4} mg/l and the predicted indirect exposure to humans through the environment was calculated to be 1.4×10^{-3} mg/man/day (i.e. 2.3×10^{-5} mg/kg/day). In Denmark, the chemical is produced, but detailed exposure information is not available, except that there is no consumer use.

For the environment, various NOEC and LC_{50} values were gained from test results; LC_{50} = 9.8 mg/l (acute fish); EC_{50} = 9.1 mg/l (acute daphnia); EC_{50} = 8.6 mg/l (acute algae); NOEC = 0.78 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to be moderately toxic to fish, daphnids and algae. The lowest chronic toxicity result, 21 d-NOEC (reproduction) of *Daphnia magna* (0.78 mg/l), was adopted for the calculation of the PNEC, applying an assessment factor of 100. Thus the PNEC of the chemical is 0.0078 mg/l. Since the PEC is lower than the PNEC, the environmental risk is presumably low.

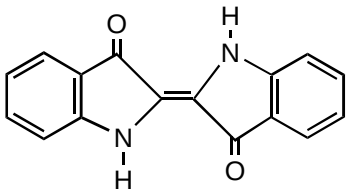
The chemical showed genotoxic effects in a chromosomal aberration test *in vitro* and in an *in vivo* micronucleus test. In a 6 months repeated dose toxicity test, the chemical showed a transient excretion of glucose to urine in the 1500 ppm group, but no other abnormalities were noted. In an OECD preliminary reproductive/developmental toxicity test, the chemical showed no effect on reproductive ability, organ weight, histopathological appearance of reproductive organs, delivery and maternal behaviour of dams, viability, clinical signs, body weight change and autopsy findings for offspring. Also, as repeated dose effect to male rats, decreased locomotor activity, prone position, bradypnea and thrombus in the kidney, heart and lung were observed in the high-dose group (300 mg/kg/day). The NOEL for 6 months repeated dose toxicity was 500 ppm (30.7 mg/kg/day) in both sexes. The NOEL for reproductive toxicity was 300 mg/kg/day and the NOEL for repeat dose toxicity to male rats in the preliminary reproductive test was 100 mg/kg/day.

3-Methyl-4-nitrophenol showed genotoxicity in an *in vitro* chromosomal aberration test. However, this chemical is used as raw material for the synthesis of pesticides in closed systems, and the results from gathering international exposure information showed that the production volume is low, and exposure to the general population from the general environment is currently low. In Japan, the chemical is manufactured and processed in a closed system, i.e. the product itself and all reagents and solvents for its synthesis are handled in perfectly closed tubes and vessels. The synthesis is operated within the same plant. At the work place, protective clothing, gloves and goggles are used. The daily intake of the chemical via the environment was estimated to be 1.4×10^{-3} mg/man/day (i.e. 2.3×10^{-5} mg/kg/day) from the result of worst-case calculation using the MNSEM 145I exposure model. The concentrations in surface water and sediments were not detectable in a Japanese environmental monitoring program. No consumer uses have been identified. Although no data on work place monitoring have been reported, voluntary exposure reducing procedures are in place in Japan. Occupational exposure seems to be low.

Therefore, 3-methyl-4-nitrophenol is considered as low priority for further work.

NATURE OF FURTHER WORK RECOMMENDED

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	482-89-3
Chemical Name	3H-Indol-3-one, 2-(1,3-dihydro-3-oxo-2H- (Indigo Blue)
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

It is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

The production volume of Indigo Blue was ca. 1,200 tonnes/year in 1990 - 1992 in Japan. This chemical is used in dyeing industry as a direct dye or as an intermediate for the synthesis of other dyes. This chemical is considered as "not readily biodegradable".

PECs have been calculated based on several models considering its physico-chemical properties (e.g. molecular weight, water solubility, vapour pressure and partition coefficient). The worst estimated concentrations were 7.7×10^{-12} mg/l (air), 2.6×10^{-4} mg/l (water), 5.1×10^{-4} mg/kg (soil), 2.2×10^{-2} mg/kg (sediment).

For the environment, various NOEC and LC_{50} values were gained from test results; LC_{50} > 1000 mg/l (acute fish); EC_{50} = 250 mg/l (acute daphnia); EC_{50} = 6.5 mg/l (acute algae); NOEC = 0.78 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to be moderately toxic to daphnids and algae. The lowest chronic toxicity result, 21 d-NOEC (reproduction) of *Daphnia magna* (0.78 mg/l), was adopted for the calculation of PNEC, applying an assessment factor of 100. Thus the PNEC for the chemical is 0.0078 mg/l. Since the PEC is lower than the PNEC, environmental risk is presumably low.

Based on the physico-chemical properties, the level exposed indirectly through the environment was estimated to be 1.9×10^{-3} mg/man/day (i.e. 3.2×10^{-5} mg/kg/day). Also, the daily intake through drinking water is estimated to be 8.7×10^{-6} mg/kg/day and through fish is calculated to be 2.2×10^{-5} mg/kg/day. No data on occupational exposure are available. Neither monitoring data at work place nor data on consumer exposure have been reported.

Although the chemical showed no genotoxic effects in bacteria, a positive result was obtained from a chromosomal aberration test *in vitro*. However, in a micronucleus test *in vivo* that was performed to confirm the mutagenicity of the chemical, the result was negative.

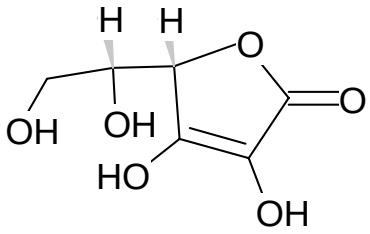
In a 2-year feed study in rats, there were no serious effects related to the test substances up to the highest dose level (3% feed i.e. approx 1200 mg/kg/day). In a 3-generation reproductive toxicity study at doses of 5, 50, 150, or 500 mg/kg/day in rats, there were also no effects observed such as reproduction performance, maternal weight gain and fetal development. Therefore, the NOEL was 1,200 mg/kg/day for repeated dose toxicity as well as 500 mg/kg/day for reproductive toxicity.

For human health, estimated dose of low concern (EDLC) was calculated as 12 mg/kg/day and 5 mg/kg/day for repeated dose and reproductive toxicity, respectively, using a safety factor of 100. Daily intake of the chemical was estimated as 3.2×10^{-5} mg/kg/day from an exposure model. Also, the daily intake through drinking water is estimated to be 8.7×10^{-6} mg/kg/day and through fish is calculated to be 2.2×10^{-5} mg/kg/day. The EDLC is quite larger than the estimated human exposure, and the margin of safety is very large. Therefore, health risk through the environment, in general, is considered to be presumably low due to its use pattern and exposure situation.

In conclusion, no further testing is needed at present considering its toxicity and exposure levels.

NATURE OF FURTHER WORK RECOMMENDED

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	50-81-7
Chemical Name	L-Ascorbic Acid
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

[X] presently of low priority for further work

[ ] requiring further information to assess identified concerns

[ ] candidate for in-depth risk assessment with a view to possible risk reduction activities

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

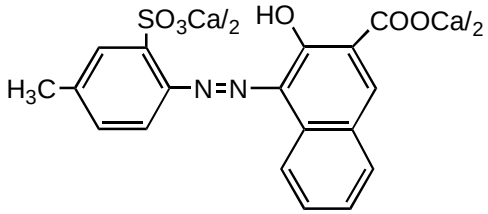
Environment - L-Ascorbic acid is of low toxicity to environmental organisms and is often naturally produced within the organism. Effects on environmental ecosystems would not be expected from the current industrial production and emissions of L-ascorbic acid, which account for only a small fraction of the L-ascorbic acid naturally present in the environment.

Human Health - Intakes of relatively high dose levels of ascorbic acid in humans (up to 1 gram per day or more) do not result in any significant adverse health effects. Animal studies support the low toxicity of this substance.

NATURE OF FURTHER WORK RECOMMENDED

none

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	5281-04-9
Chemical Name	2-Naphthalenecarboxylic acid, 3-hydroxy-4-[(4- methyl-2-sulfophenyl)azo]-, calcium salt (D & C Red No.7)
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

It is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Exposure

D & C Red No.7 is a stable solid. Its production volume was ca. 4,400 tonnes/year in 1990 – 1992 in Japan. This chemical is used in printing inks and plastic industries in open and closed systems. This chemical is stable in neutral, acidic or alkaline solutions, and is considered as “not readily biodegradable”.

PECs have been calculated based on several models considering its physico-chemical properties (e.g. molecular weight, water solubility, vapour pressure and partition coefficient). The estimated concentrations were 6.6×10^{-9} mg/l (air), 1.0×10^{-4} mg/l (water), 5.2×10^{-7} mg/kg (soil), and 1.1×10^{-3} mg/kg (sediment). Neither monitoring data in the workplace nor consumer exposure data have been reported. Based on the physico-chemical properties, the level of indirect exposure through the environment was estimated as 3.7×10^{-4} mg/man/day (i.e. 6.2×10^{-6} mg/kg/day. The daily intake through drinking water is estimated as 3.3×10^{-6} mg/kg/day and through fish is calculated as 6.0×10^{-7} mg/kg/day. No data on occupational exposure are available.

Environment

For the environment, various NOEC and LC_{50} values were gained from test results; LC_{50} = 33 mg/l (acute fish); EC_{50} = 280 mg/l (acute daphnia); EC_{50} = 190 mg/l (acute algae); NOEC = 3.0 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to be slightly toxic to fish. The lowest chronic toxicity result for daphnids [21d-NOEC (reproduction) of *Daphnia magna* (3.0 mg/l)] was used with an assessment factor of 100 to determine the PNEC according to the OECD Provisional Guidance for Initial Assessment of Aquatic Effects. Thus, the PNEC of the chemical is 0.03 mg/l in the present report. The PEC is lower than the PNEC, therefore the environmental risk is presumably low.

Human Health

The chemical showed no genotoxic effects in bacteria and chromosomal aberration tests *in vitro*. In a combined repeat dose and reproductive/developmental toxicity screening test, increases of kidney weights and decreases of thymus weights were observed in parental animals at the highest dose (1000 mg/kg/day). At the terminal necropsy, gross changes included a small thymus up to the lowest dose (100 mg/kg/day). In the histopathological examinations, regenerated renal tubular epitheliums were also seen at the middle dose (300 mg/kg/day) and at the highest. Regarding reproductive/developmental end-points, there were no effects observed related to mating, fertility and the oestrus cycle and there were no effects observed in dams during the pregnancy and lactation period. Therefore, the NOEL was less than 100 mg/kg/day for repeated dose toxicity and than 1000 mg/kg/day for reproductive toxicity.

As for indirect exposure via the environment, the daily intake through drinking water is estimated as 3.3×10^{-6} mg/kg/day and through fish is calculated as 6.0×10^{-7} mg/kg/day. For human health, although NOEL is estimated as less than 100 mg/kg/day for repeated dose and 1,000 mg/kg/day for reproductive toxicity, the margin of safety is very large. Therefore, the health risk through the environment, in general, is considered to be presumably low due to the chemical's use pattern and exposure.

In conclusion, no further testing is needed at present considering its toxicity and exposure levels.

NATURE OF FURTHER WORK RECOMMENDED

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	75-86-5
Chemical Name	Acetone cyanohydrin
Structural Formula	$(CH_3)_2C(OH)CN$

CONCLUSIONS AND RECOMMENDATIONS

[X] presently of low priority for further work

[ ] requiring further information to assess identified concerns

[ ] candidate for in-depth risk assessment with a view to possible risk reduction activities

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

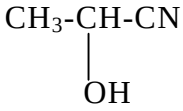
Environment -The toxicity of acetone cyanohydrins is believed to be predominantly attributable to dissociation of the cyanide molecule with the resultant formation of molecular (undissociated) hydrocyanic acid. Hydrocyanic acid, by virtue of its small size and lack of charge, readily penetrates the external membranes of aquatic organisms (Doudoroff, 1976) and inhibits respiration. Any potential environmental problems would be caused by cyanide rather than the parent compound.
There are no data on the environmental concentrations of acetone cyanohydrins and there is no basis to model environmental concentrations from release since the compound is an intermediate which rapidly dissociates, and is manufactured and used in enclosed systems. Therefore, it is difficult to interpret the PNEC. However, the rapid dissociation and tight controls on the release of acetone cyanohydrin mean that it is unlikely that the PNEC will be attained.
Therefore, it would appear that acetone cyanohydrin represents little risk to the environment under current production and use. No further work is recommended.

Human Health – The rapid formation of hydrogen cyanide from acetone cyanohydrin is of concern, and the critical adverse health effect is acute lethality. However, at anticipated levels of human exposure no systemic effects are likely to occur. The chemical is not genotoxic or toxic to development or the reproductive system.
No further toxicity tests are required. Depending on workplace exposure assessments at individual sites protective measures may need to be increased.

NATURE OF FURTHER WORK RECOMMENDED

No further work is required.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	78-97-7
Chemical Name	2-Hydroxypropanenitrile
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

It is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

The production volume of 2-hydroxypropanenitrile was ca. 11,000 tonnes/year in 1990 - 1993 in Japan. This chemical is used as an intermediate for the production of lactic acid, alanine, acrylic fibres and resins in closed systems in Japan. Also, it is used as and intermediate for acrylic acid and resins in Europe. This chemical is stable in neutral or acidic solutions, it is unstable in alkaline solution, and it is considered as "readily biodegradable".

PECs have been calculated based on fugacity level III models considering its physico-chemical properties (e.g. molecular weight, water solubility, vapour pressure and partition coefficient). The worst estimated concentrations were 7.0×10^{-8} mg/l (air), 6.7×10^{-5} mg/l (water), 3.7×10^{-4} mg/kg (soil), 1.2×10^{-4} mg/kg (sediment).

No monitoring data at the work place are available. As the chemical is used in closed systems, so far no data for consumer use are available. Based on the physico-chemical properties, the level exposed indirectly through the environment was estimated as 3.2×10^{-3} mg/man/day. The daily intake through drinking water is estimated as 1.3 x 10^{-4} mg/man/day and through fish is calculated as 2.2 x 10^{-6} mg/man/day.

For the environment, various NOEC and LC_{50} values were gained from test results; LC_{50} = 0.98 - 1.1 mg/l (acute fish); EC_{50} = 17 mg/l (acute daphnia); EC_{50} = 0.14 mg/l (acute algae); NOEC = 0.17 mg/l (long-term daphnia reproduction). Based on these values, the PNEC was estimated to be 0.0017 mg/l for aquatic organisms. Although the chemical is strongly toxic to fish and algae and moderately toxic to daphnids, PEC/PNEC ratio is less than 1. Therefore, it is considered to be of low risk for the environment.

Although the chemical showed no genotoxic effects in bacteria, weakly positive result was obtained in a chromosomal aberration test *in vitro*.

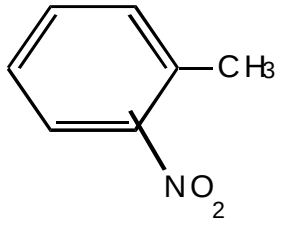
In a combined repeat dose and reproductive/developmental toxicity screening test, transient hypolocomotion, hypopnea and salivation were found at the highest dose (30 mg/kg/d) in both sexes. Increased liver weights occurred in the highest male group. In a pathological examination, enlargement of the liver was also observed in the same group. Such hepato-toxic effects were revealed to be due to a centrilobular hypertrophy and a fatty change of hepatocytes in a historical examination. For reproductive/developmental toxicity end-points, there were no effects observed concerning mating, fertility and oestrus cycle and also for dams during the pregnancy and lactation period. Therefore, NOEL was 6 mg/kg/day for repeated dose toxicity and 30 mg/kg/day for reproductive toxicity.

As for indirect exposure via environment, the daily intake through drinking water is estimated as 1.3×10^{-4} mg/man/day and through fish is calculated as 2.2×10^{-6} mg/man/day. The margin of safety is very large. Therefore, health risk through the environment, in general, is considered to be low due to its use pattern and exposure situation.

In conclusion, no further testing is needed at present considering its toxicity and exposure levels.

NATURE OF FURTHER WORK RECOMMENDED

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	88-72-2
Chemical Name	*o*-Nitrotoluene
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

Potential for risk to man due to genotoxicity and thus presumed carcinogenicity. Some difficulties over classification based on mesotheliomas in 90-day study and Sweden has requested this be considered urgently.

Manufacturers should be contacted regarding product stewardship and the preparation of a status report.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

2-Nitrotoluene (2NT) is predominately used as raw material for the synthesis of explosives, pharmaceuticals, colourants, dyes, rubber, petrochemicals and pesticides. A single non-reactant use of 2-NT as a solvent in pigment manufacturing process is identified. 2NT has not been identified in consumer products.

2NT may enter the environment via the air and waste water emissions during its production and/or use as a reactant in the production of products. If released to soil, 2NT may be resistant to oxidation and chemical hydrolysis. 2NT is predicted to be moderately to highly mobile in soil and volatilise slowly from dry soil surfaces. If released to water, 2NT may be subject to direct photolysis, indirect photolysis (half life < 1 hour), volatilisation (half life, 21 hours) and possibly aerobic biodegradation (with acclimation). Based upon monitoring data, the half life of 2NT in a river 4-5m deep has been estimated to be 3.2 days. If released to the atmosphere, 2NT is expected to exist entirely in the vapour phase, with the principle removal mechanisms being reaction with hyrdoxyl radicals. (half life 8 hours) and direct photolysis. BCF values of 100, 33 and 16 have been calculated, and taken in consideration with the log Pow value of 2.3, it is expected that 2NT would not significantly bioaccumulate in aquatic organisms.

The anticipated ecotoxicological hazards posed by 2NT are low/moderate acute and chronic toxicity to aquatic and terrestrial organisms. The MTC (maximum tolerable concentration) for aquatic organisms has been calculated from the lowest observed NOEC, 0.5 mg/l (*Daphnia magna*). Using an assessment factor of 10 the derived MTC_{aq} is 0.050 mg/l = 50 µg/l. For environmental risk, local "worst case" PECs have been calculated for a single factory scenario under climatical conditions expected to be normal at a Swedish production/processing site. The calculated PECs are: for air =< 1.5×10^{-4} mg/m^3; soil =< 0.043 µg/l; water =< 9.2 µg/l, and; sediment =< 23 µg/l. Local PEC/MTC estimates indicate that 2NT may not cause effects upon organisms in the aquatic environment.

In animal studies 2NT was not corrosive or irritating to the rabbit skin and eye(s). Studies concerning the skin sensitisation potential of the substance have not been located.

2NT is moderately toxic by the oral route but only slightly toxic by the inhalatory and dermal routes. Repeat dose toxicity studies have been performed via the oral route. Effects on the liver, kidney, reproductive system, lung and haematopoietic/splenic system have been observed in rats and on the liver and nasal cavity in mice. In repeated dose studies hepatotoxicity was considered the most sensitive toxicological marker and LOAEL is set at 45 mg/kg for rats and NOAEL at 104 mg/kg for mice.

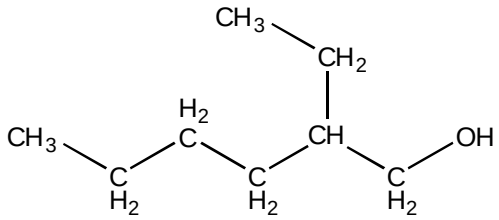
2NT was negative in *Salmonella* mutagenicity test and *in vitro* chromosomal aberration test but produced SCE in the presence of metabolic activation. *In vivo*, 2NT was genotoxic (UDS; covalent binding). An *in vivo* chromosomal aberration study is not available. A 13 week study demonstrated 2NT to be a potential carcinogen in rats.

In a "Preliminary Screening Test" effects on reproduction were not observed (histopathological findings were not documented). A teratology study has not been located. In general, 2NT is more toxic than its 3- and 4- nito isomers. Documented symptoms for humans are headache, flushing of face; dizziness, dyspne, cyanosis, nausea, vomiting, muscular weakness, increased pulse and respiratory rate, irritability and convulsions. 2NT is also a methaemoglobin former apparently of low grade. Target organs for nitrotoluene isomers are identified as the blood, central nervous system, gastrointestinal, cardiovascular system, and skin.

NATURE OF FURTHER WORK RECOMMENDED

Manufacturers should be contacted regarding product stewardship and the preparation of a status report.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	104-76-7
Chemical Name	2-Ethylhexanol
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

This chemical is a candidate for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

1.7 millions tonnes of 2-Ethylhexanol (2EH) was produced in 1992 worldwide. 2EH is predominantly used as raw material (intermediate) in the synthesis of platicizers, hexyl esters and acrylates and has other uses e.g. in paints.

2EH is classified as “inherently biodegradable”, and may have a high potential to bioaccumulate in aquatic organisms. 2EH is of moderate acute toxicity to aquatic animals and plants (L(E)C50 within 11.5-44mg/l). Data on chronic toxicity on aquatic animals is not available.

Calculations based upon chemical/physical data indicate that 2EH will migrate to the water compartment. 2EH will only degrade slowly in water, and is expected to be persistent in ground water. 2EH will degrade in the air.

Information is not available on degradation in soil.

The potential exposure of the local aquatic environment around the factory site is considered to be low if the waste water is effectively treated. It is unclear if the use of WWTP adapted to 2EH satisfactorily reduces the concentration of 2EH in the sludge and effluent. Without proper treatment of waste water the PEC/PNEC (>1) indicates a possible risk to the aquatic environment. Monitoring data indicates that such an exposure does occur.

2EH was moderately irritating to rabbit skin and a moderate-to-severe irritant to the eye in rabbits. A sensitization study is not available.

2EH is rapidly and extensively absorbed via the gastrointestinal tract in rats and rabbit. Percutaneous absorption through rat skin is low. Observed toxicity via p.o. and inhalation routes indicates that 2EH/metabolites are distributed to several organs. Target organs include liver, kidney and stomach. The excretion of 2EH/metabolites following p.o. administration is rapid and extensive occurring mainly via the urine in rat and rabbit.

Acute oral studies (rat, mouse, guinea pig, rabbit) indicate moderate-to medium toxicity (>3000-600mg/kg). Medium acute toxicity is indicated in inhalation studies (≥1.2-<5.3mg/l). Acute dermal toxicity was moderate in rat and rabbit (>2000mg/kg). Intraperitoneal administration causes high acute toxicity. (CNS was a target but long-term studies

show effects indicative of CNS toxicity were few.)

Repeat dose 90-day toxicity studies have been performed (via the oral route (rat, mouse), inhalation route (rat)). Effects on the liver, stomach, and kidney degeneration were reported. For oral exposure NOAEL is 125mg/kg/d (rat), inhalation NOAEL is ≥0.639mg/l/d. For dermal route subacute studies are available and the NOAEL is <1.66 g/kg/d.

2EH was negative in Salmonella mutagenicity tests and chromosomal aberration tests (*in vitro* and *in vivo*). Other studies indicate that 2EH does not have genotoxic activity and carcinogenic potential was not demonstrated in studies in rats and mice. NOAELrat = 50mg/kg.

Fertility studies are not available, however several oral subacute studies in rat and mice have produced alterations in testicular weight. This was not observed with rats and mice in 90-day repeat dose studies.

Developmental studies are available for rats (oral, dermal, inhalation) and mice (oral). Effects were only observed for rats treated by the oral route and included skeletal malformation and retardation. The NOAELrat,oral = 130 mg/kg, the NOAELrat,inhal = <0.85 mg/l, the NOAELrat,dermal = 840mg/kg and the NOAELmouse, oral = 191 mg/kg.

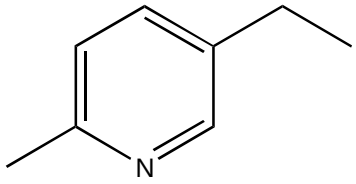
Analysis of the available data show that for an indirect, consumer or occupational setting the margin of safety for man is high.

NATURE OF FURTHER WORK RECOMMENDED

Currently considered that further Post-SIDS work is needed.

Look at with 2-Ethylhexanoic acid (149-57-5), especially regarding the reprotoxicity end-point, exposure and other data from long-term ecotoxicity tests.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	104-90-5
Chemical Name	5-Ethyl-2-picoline
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

This chemical is currently of low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

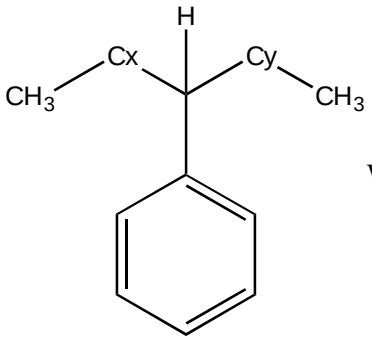
This chemical was produced in the range of 10,000-50,000 tonnes in 1992. This chemical is mainly used as an industrial intermediate for the production of nicotinic acid and nicotinamide. This chemical may be released to water and air during production and filling processes. In surface water this chemical will degrade and will not bioconcentrate in fish. In air the substance is degraded quite rapidly.

This chemical has a log Pow<3, a relatively high water solubility and is degradable. The lowest aquatic effect concentrations were determined with algae (NOEC(72h): 0.689mg/l). Applying an assessment factor of 10 the resulting PNEC is 0.0689mg/l. This value has to be compared with that derived from the lowest toxicity value of the acute tests (biomass algae: EC50(72h): 30.6mg/l). An assessment factor of 100 has to be chosen when L(E)C50 values for all three taxonomic groups are available. With this assessment factor the PNEC is 0.31mg/l. Comparing the two derived PEC values (0.002mg/l and 0.03mg/l) with the lower PNEC of 0.0689 mg/l gives PEC/PNEC ratios of 0.03 and 0.44. This chemical is of moderate acute toxicity, is not genotoxic, has to be classified as corrosive and has no effect on the general reproductive performance of test animals. Based on the NOEL of 30mg/kg/day from the 28-days oral toxicity study in rats, the estimated dose of low concern (EDLC) can be calculated taking into account an uncertainly factor (UF) of 100, so 0.3 mg/kg/day. EDLC/EHEocc = 37.5.

The results of occupational exposure do not give cause for concern, and no hazard to human health exists for the general population in the vicinity of the plant.

NATURE OF FURTHER WORK RECOMMENDED

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	123-01-3 and 6742-54-7
Chemical Name	Benzene, C10-C16 Alkyl derivatives
Structural Formula	 Where x + y = 7 - 13 and x = 0 - 6

CONCLUSIONS AND RECOMMENDATIONS

This group of chemicals is currently of low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Attention: This chemical is to be discussed with 6742-54-7, 68442-69-3, 68648-87-3, 129813-58-7, 129813-59-8 and 129813-60-1 as a group of Alkylbenzenes.

Dodecylbenzene (123-01-3) and undecylbenzene (6742-54-7) are not produced in significant commercial quantity as pure materials. Manufacturers produce various mixtures of long-chain linear alkybenzenes with the alkyl group containing from 10 to 16 carbon atoms.

The production of linear alkylbenzene sulfonate (LAS), a detergent surfactant, consumes greater that 98% of all linear alkylbenzenes. The potential for employee exposure is limited and infrequent. The low vapor pressure and controls utilized for other materials used in the process limits the emission of liner alkylbenzenes to air.

Linear alkylbenzenes undergo rapid primary biodegradation in natural waters and complete mineralization by microorganisms under aerobic conditions and in sludge amended soils. Due to their metabolism, these materials possess little potential to bioconcentrate in fish. They do not appear to undergo direct photolysis or chemical change in the environment.

Linear alkylbenzene, at various concentrations up to and exceeding their approximate water solubility limits, had no acute effects on all the species tested, except *Daphnia magna*. Linear alkylbenzene is 10 times more toxic to Daphnids than fish in acute tests.

Linear alkylbenzenes are not acutely toxic. Data from repeat exposure, reproductive and genotoxicity studies also indicate a low potential for toxic effects.

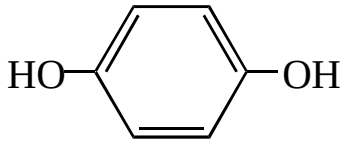
The levels of both consumer and occupational exposure are expected to be very low based on their physical and

chemical properties, use and handling patterns.

NATURE OF FURTHER WORK RECOMMENDED

No need for further work.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	123-31-9
Chemical Name	Hydroquinone
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

It was reported that the chemical was of low international concern, but processing sites such as in industrial photography, may present local environmental concern based on default modelling.

It is currently considered of low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Virtually all the uses of hydroquinone are industrial. Approximately 25% of the hydroquinone manufactured is used as an intermediate for synthesis of antioxidants and antiozonants for use in rubber. Another 25% is used as an intermediate for chemical conversion to inhibitors used to stabilize monomers. An additional 33% is used in the photographic industry including black-and-white photographic film, lithography, and hospital x-ray film. Other uses (11-12%) include chemical conversion to stabilizers for paints, varnishes, motor oils, and fuels, and for antioxidants for industrial fats and oils. Hydroquinone has been used in water cooling towers as a rust inhibitor. Hydroquinone is considered to be readily biodegrable and photodegradable.

The aquatic toxicity of hydroquinone to fresh water fish, Daphnia, and algae was between 0.050-0.335 mg/l; the predicted chronic values for these fresh water taxa were calculated to be < 0.100. The 84 hr LC_{50} for the salt water shrimp, *C. septemspinosa*, was selected as the only salt water species for analysis. Based on these data and on the predicted aquatic toxicity values, the US EPA identified concern concentrations or predicted no effect concentrations (PNECs) at 1.0 µg/l for fresh water species and 8.0 µg/l for salt water species. Alternatively, a PNEC can be derived using the assessment factors recommended in the SIDS Manual. As only acute effect data for fish and daphnids are available, an assessment factor of 100-1000 would be appropriate. Due to the large available database, a factor of 100 would be acceptable. Applied to the lowest experimental value of 0.044 mg/l (fathead minnow), a PNEC of 0.44 µg/l can be derived.

The PNECs are compared to the maximum annual estimated water concentrations based on the 1992 TRI release levels and the "what-if scenarios" for manufacturing, processing, and use sites which were considered to be conservative estimates of PECs.

All but one of the direct discharge sites have PECs less than 0.07 µg/l and, therefore, the PEC/PNEC ratios range from 8.2×10^{-5} to 6.8×10^{-2} using a PNEC of 1.0 µg/l. One direct discharger has a predicted surface water concentration of 180 µg/l which would indicate a PEC/PNEC ratio of greater than one. However, in investigating site specific information for this discharger, it became apparent that the plant PEC/PNEC ratio was significantly less than 1 as no hydroquinone was detected from its NPDES-regulated outfall prior to discharge.

Use of the alternative PNEC of 0.44 μg/l causes an additional four indirect discharges to exceed a PEC/PNEC ratio of one (PEC/PNEC ratios of 1.5-2.0); however, considering that there are estimated to be 16,000 to 66,000 processor/users of hydroquinone in the USA, the number of predicted PEC/PNEC ratios > 1 are small. Since all of the direct and indirect discharges identified in the exposure assessment have NPDES regulated discharges, it is very unlikely that they actually have discharges with PEC/PNEC ratios > 1. It is much more likely that the "what-if scenario" has overestimated the actual PEC.

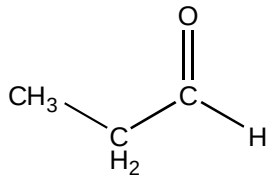
The frequency of exceeding a PEC/NPEC of 1 can be calculated using the Probabilistic Dilution Model (PDM 3) program. Using this model, a concern concentration of 1 μg/l is predicted to be exceeded 0.5 days/yr (0.14% of the year) and a concern level of 0.044 μg/l is predicted to be exceeded 3 days/yr (0.81% of the year).

While toxicity to mammalian species is associated with high doses of hydroquinone, these effects are either species- and strain-specific or minimized in humans through reduced exposure. Dermal effects in humans who use hydroquinone-containing skin products appear to be limited to individuals who misuse the products or to products which contain other active ingredients. Similar dermal effects have not been demonstrated in animals treated with similar or higher concentrations of hydroquinone. Potential hazards from dermal exposure to aqueous solutions of hydroquinone are also low based on dermal absorption rates. Exposure information provided indicates that exposure potential for hydroquinone is low. Because no human health concerns have been identified and exposure potential is low, this substance has a low priority for further work.

NATURE OF FURTHER WORK RECOMMENDED

Depending on the extent of use, national action to avoid risk to the aquatic environment could be warranted on some site-specific conditions.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	123-38-6
Chemical Name	Propanal
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

This chemical is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

The estimated annual production of propanal in the United States is in the order of 275 million pounds. Worldwide, it is estimated that 405 million pounds of this aldehyde are produced annually. Although propanal is a high production volume chemical, it finds use almost solely as a chemical intermediate.

Production and conversion to other chemicals necessarily take place in closed systems because of the extremely volatile nature of this chemical. U.S. TRI reporting requirements indicate that sizable fugitive emissions exist (988,986 pounds of propanal into the air, 34,885 pounds to other segments of the environment in 1990). However, propanal has a relatively short existence in air ($T_{1/2} \approx 6$ hours). In addition, the chemical will tend to partition from air into water. It is easily oxidized to propionic acid, a natural constituent of nature, which can be metabolized in biological organisms by the enzymatic pathways of intermediary metabolism.

Propanal has been shown to be moderately toxic to fish (LC50 = 15 mg/l [14d]), algae (EC50 = 40 mg/l [96h]), and of low order of toxicity to daphnia (EC50 = 125mg/l [48h]). The aldehyde has been shown to be at most only a slight threat to water treatment plants based on toxicity to bacteria. A single study demonstrates that propanal can inhibit the germination of seeds, but only at relatively high concentrations.

This chemical is highly soluble in water and has an octanol/water partition coefficient of less than 1. Based on the physical and chemical properties, the chemical will not be a persistent environmental contaminant. Episodic accidental spills into ponds and streams would pose a moderate environmental threat. Considering rapid oxidation to propionic acid and its low order of toxicity, this threat would be temporary in nature. Therefore, environmental risk is considered to be low.

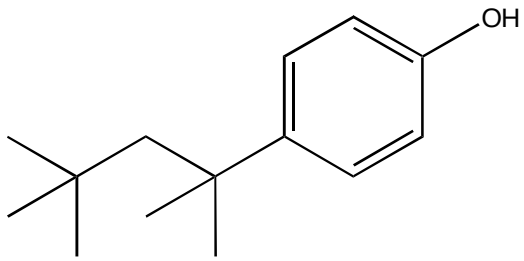
Propanal is produced and used exclusively in closed systems and transported by bulk carrier. These conditions predicate low exposure of personnel in the work place. This assumption is supported by industrial hygiene monitoring data which indicate a large portion of samples are below the detection limit of 0.01 ppm and exposures very rarely exceed 1 ppm. Considering the very low concentrations of propanal measured within production facilities, air concentrations at the fence line and within the surrounding community must be extremely low. Propanal is not directly used in products reaching the consumer. Because of its reactive nature and volatility, residual concentration of propanal in consumer products is very low.

Basic toxicology studies provide data to sufficiently identify the most sensitive toxic effect of propanal, irritation upon direct contact with tissues, particularly irritation of mucosa of the upper respiratory tract upon exposure to vapor. This observation is consistent with the known irritant effects of other short chain alkyl aldehydes. It does not have specific adverse effects on the reproductive capabilities of either male or female rats, and does not produce specific adverse effects on the developing offspring of laboratory animals. This aldehyde has exhibited weak genotoxic activity in some *in vitro* assay systems, this is consistent with what has been observed with other short-chain alkyl aldehydes.

Considering all of the above, propanal is considered to be of low potential risk and low priority for further work.

NATURE OF FURTHER WORK RECOMMENDED

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	140-66-9
Chemical Name	Phenol, 4-(1,1,3,3-tetramethylbutyl)-
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

The chemical is currently considered as requiring further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

In 1993 (Switzerland), produced or imported 377t Phenol, 4-(1,1,3,3-tetramethylbutyl)- (OP) (of this, 129 t was imported). In the US conservative production volume estimates indicate 5400-32200 t/year. OP is manufactured by catalytic reaction of Phenol with Diisobutylene. The OP is directly transferred from the reactor to a reservoir via pipes and from there to heated railway tankers. Most of OP appears to be used as an intermediate for the production of resins, non-ionic surfactants and rubber additives.

OP is biodegradable. In the surface layer of natural waters 30% of OP can be degraded within one day. OP is acutely very toxic to aquatic organisms and may cause long-term adverse effects in the aquatic environment. The environmental hazard assessments with the available exposure data shows that OP may represent a risk to the hydrosphere. The main reason for this risk is not the use of OP itself, but the use of Octylphenol-ethoxylates which may be degraded back to OP in the aquatic environment.

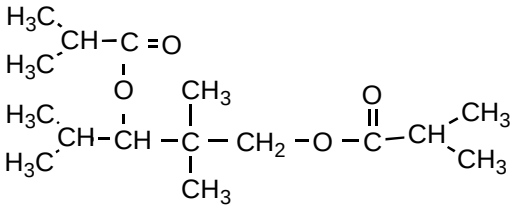
OP is not acutely toxic to human health, but is slightly irritating to the skin and highly irritating to the eyes. It is not genotoxic, but may cause depigmentation of the skin. *In vitro* studies showed that OP may displace 17-β-estradiol from its receptors in a competitive manner and can promote cell proliferation in estrogen dependent cells.

The available data indicate that OP does not give cause for concern for human health.

NATURE OF FURTHER WORK RECOMMENDED

Further testing or analysis of exposure information to assess identified concerns. The assessment of nonylphenol (CAS Nos 84852-15-3 & 25145-52-3) within the OECD HPV Chemicals Programme should be taken into account.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	6846-50-0
Chemical Name	2,2,4-Trimethyl-1,3-pentanediol diisobutyrate
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

It is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

2,2,4-Trimethyl-1,3-pentanediol diisobutyrate is stable liquid and the production volume is ca. 1,200 tonnes/year in 1990 - 1993 in Japan. This chemical is used as additives to plastic (plasticizer). This chemical is stable in neutral and acidic solutions, and is considered as “inherently biodegradable”.

PECs have been calculated based on an emission and effluent scenario and a dilution factor. $PECs_{local}$ for the aquatic compartment were 5.1×10^{-11} and 1.3×10^{-8} mg/l.

For the environment, various NOEC and LC_{50} values were gained from test results; LC_{50} = 18 mg/l (acute fish); EC_{50} = 300 mg/l (acute daphnia); EC_{50} = 8.0 mg/l (acute algae); NOEC = 5.3 mg/l (acute algae); NOEC = 3.2 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to be moderately toxic to algae and daphnids, and slightly toxic to fish. The lowest chronic toxicity data to daphnia, 21d-NOEC (reproduction) of *Daphnia magna* (3.2 mg/l) was adopted for the calculation of PNEC. An assessment factor of 100 was used to both acute and chronic toxicity data to determine PNEC according to the OECD Provisional Guidance for Initial Assessment of Aquatic Effects. Thus, PNEC of the chemical is 0.032 mg/l. The PEC is lower than the PNEC, therefore the environmental risk is presumably low.

Neither monitoring data at work place nor consumer exposure have been reported. Based on the physico-chemical properties and a calculation model, the level exposed indirectly through the environment was estimated as 9.3×10^{-4} mg/man/day. . The daily intake through drinking water is estimated as 4.2×10^{-7} mg/kg/day and through fish is calculated as 1.5×10^{-5} mg/kg/day.

The chemical showed no genotoxic effects in bacteria and chromosomal aberration test *in vitro*.

In a combined repeat dose and reproductive/developmental toxicity screening test, increase of liver and kidney weights were observed in parental animals from the middle dose level (150 mg/kg/day). In the histopathological examinations, increases in grade of basophilic change of renal tubular epithelium and degeneration of hyaline droplet were observed from the same level. In addition, necrosis and other renal effects were also observed. From the view point of reproductive/developmental end-points, there were no effects observed related to mating, fertility and

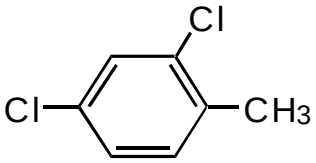
oestrus cycle and also for dams during the pregnancy and lactation period and for pups after their birth. Therefore, NOEL was 30 mg/kg/day for repeated dose toxicity as well as 750 mg/kg/day for reproductive toxicity.

As for indirect exposure via the environment, the daily intake through drinking water is estimated as 4.2×10^{-7} mg/kg/day and through fish is calculated as 1.5×10^{-5} mg/kg/day. The margin of safety is very large. Therefore, health risk through the environment, in general, is considered to be presumably low due to its use pattern and exposure situation.

In conclusion, no further testing is needed at present considering its toxicity and exposure levels.

NATURE OF FURTHER WORK RECOMMENDED

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	95-73-8
Chemical Name	2,4-Dichlorotoluene
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

It is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Exposure

2,4-Dichlorotoluene is volatile liquid and the production volume is ca. 900 tonnes/year in 1990 – 1992 in Japan and 10,000 - 20,000 tones/year in 1984 in the EEC. This chemical is used as an intermediate for pesticides, drugs and chlorinated-nitrated benzenes in closed systems in Japan. This chemical is stable in neutral, acidic or alkaline solution, and is considered to be “not readily biodegradable”.

PECs have been calculated based on several models considering its physico-chemical properties (e.g. molecular weight, water solubility, vapour pressure and partition coefficient). The worst estimated concentrations were 1.0×10^{-8} mg/l (air), 2.5×10^{-6} mg/l (water), 9.3×10^{-4} mg/kg (soil), 1.2×10^{-3} mg/kg (sediment). A PEC_{local} was also calculated as 6.0×10^{-8} mg/l, based on a default scenario.

No monitoring data at the work place have been available. The chemical is manufactured in a closed system and is used as an intermediate for medicines etc. There are cases where the feeding to tanks and the filling are performed in open systems, but in these cases protective masks, gloves and goggles are used. So far no uses for consumers are known. Based on the physico-chemical properties, the level exposed indirectly through the environment was estimated as 3.4×10^{-4} mg/man/day. The daily intake through drinking water is estimated as 8.3×10^{-8} mg/kg/day and through fish is calculated as 2.1×10^{-6} mg/kg/day.

Environment

For the environment, various NOEC and LC_{50} values were gained from test results; 96h LC_{50} = 2.7 mg/l (acute fish); 24h EC_{50} = 19 mg/l (acute daphnia); 72h EC_{50} = 9.7 mg/l (acute algae); 21d NOEC = 2.0 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to be moderately toxic to fish and algae and slightly toxic to daphnids. As the lowest chronic toxicity data, the 21d-NOEC (reproduction) of *Daphnia magna* (2.0 mg/l) was adopted. An assessment factor of 100 was used to both acute and chronic toxicity data to determine PNEC according to the OECD Provisional Guidance for Initial Assessment of Aquatic Effects. Thus, the PNEC of the chemical is 0.02 mg/l in the present report. The PEC is lower than the PNEC. The environmental risk is presumably low.

Human Health

The chemical showed no genotoxic effects in bacteria and in a chromosomal aberration test *in vitro*.

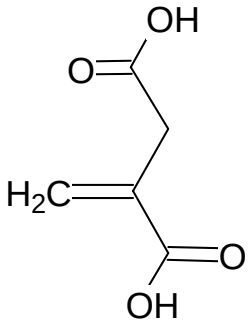
In a combined repeat dose and reproductive/developmental toxicity screening test, dose dependent salivation was found in all treated groups. Toxicological significant changes in haematological and blood chemical examinations were found at the highest dose (e.g. decrease of platelet count). Increased liver and kidney weights were also found at the same level with pathological remarks (e.g. centrilobular swelling of hepatocytes). For reproductive/developmental end-points, a decrease of fertility was found in conjunction with normal copulation but with low pregnancy at the highest dose. However, no histopathological change related to infertility was seen in the paternal organs. Decreases of pup body weights were noted in the highest dose group during the lactation period. Therefore, the overall NOEL was less than 12.5 mg/kg/day for repeated dose toxicity and 79 mg/kg/day for reproductive toxicity.

As for indirect exposure via environment, the daily intake through drinking water is estimated to be 8.3×10^{-8} mg/kg/day and through fish is calculated as 2.1×10^{-6} mg/kg/day. The margin of safety is large. Therefore, health risk through the environment, in general, is considered to be presumably low due to its use pattern and exposure situation.

In conclusion, no further testing is needed at present considering its toxicity and exposure levels.

NATURE OF FURTHER WORK RECOMMENDED

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	97-65-4
Chemical Name	Butanedioic acid, methylene
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

[X] presently of low priority for further work

[ ] requiring further information to assess identified concerns

[ ] candidate for in-depth risk assessment with a view to possible risk reduction activities

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

The worldwide production of butanedioic acid, methylene is about 15 000 tonnes per year. It is used as a comonomer for synthesis of acrylic fibers and latex.

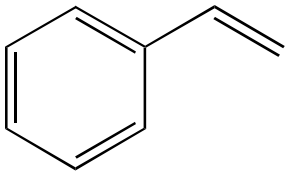
From the comparison of PEC and NEC in aquatic and terrestrial compartments, it can be concluded that the chemical is of no concern for the environment.

Normal industrial hygiene practice should adequately protect the worker in itaconic production and use facilities.

NATURE OF FURTHER WORK RECOMMENDED

none

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	100-42-5
Chemical Name	Styrene
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

The chemical is a candidate for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Worldwide production of styrene was approximately 14 million tonnes in 1992. Industry has estimated styrene production and use in Western Europe in 1993 as 3.7 million tonnes. Styrene is used primarily as an intermediate in the chemical industry. Specific uses include as a monomer in the production of polystyrene and styrene copolymers, styrene-butadiene rubbers and in unsaturated polyester resins.

Styrene reacts readily with hydroxyl radicals and with ozone in the atmosphere, with an estimated half-life of 4 hours. It has a low potential for the generation of low-level ozone. Styrene is readily biodegradable under aerobic conditions. Due to its high vapour pressure and low to moderate solubility, volatilisation from water is likely to be an important distribution process. From its octanol-water partition coefficient (K_{ow}) value, styrene is predicted to be moderately mobile in soils. The K_{ow} value also indicates a potential for bioaccumulation, but by analogy with other substances such as toluene, xylene and ethylbenzene it does not appear likely that styrene will accumulate in aquatic organisms.

Styrene has moderate toxicity to aquatic organisms. Different organisms show a similar sensitivity to styrene in acute tests: fathead minnow 96 hour LC_{50} 4.02 mg/l; *Daphnia magna* 48 hour EC_{50} 4.7 mg/l; amphipod *Hyallela azteca* 96 hour LC_{50} 9.5 mg/l; algae *Selenastrum capricornutum* 72 hour EC_{50} 4.9 mg/l. Following a detailed risk assessment in the European Union, this chemical is currently considered of low priority for further work for the environment.

Styrene is generally of low acute toxicity in experimental animals (with the exception of the mouse) and humans. Single exposure to styrene has the potential to produce CNS depression at high concentrations (800 ppm) in animals and humans. Liquid styrene is irritating to the skin and both the liquid and vapour are irritating to the eyes. The animal sensitisation data are inadequate. However, given that widespread exposure to styrene has led to only one reported possible case of skin sensitisation, this extensive experience appears to indicate that styrene is not a skin sensitiser. Similarly, there has been extensive inhalation exposure in humans, which has resulted in only two case reports of asthma, each of which has unconvincing aspects to it. This suggests that styrene is not a respiratory sensitiser.

There is a considerable database on the effects of repeated exposure to styrene in humans and experimental models. Neurotoxicity is a key issue and no agreement was reached at the SIAM on the interpretation of neurotoxicity studies

in humans. The database is of mixed quality and a precise threshold for health effects cannot be easily identified from human studies. The animal data indicate a NOAEL of 200 ppm in repeated exposure studies in the rat. A histopathological change in the olfactory epithelium indicating respiratory tract irritation was observed at concentrations of 500 ppm and above. At a higher concentration (800 ppm) damage to the auditory system (hair cell loss), with associated functional impairment, was observed. Although extensive information is available on genotoxicity and carcinogenicity, no agreement of the interpretation could be reached at the SIAM. However, it was recommended that a second *in vivo* genotoxicity study would perhaps provide reassurance.

No adequate fertility studies are available. The only available study indicated no effects on fertility were observed at low doses. However, a well conducted 90-day repeated exposure study in rats revealed no evidence of testicular effects at airborne concentrations up to 1500 ppm. In a well-conducted developmental toxicity study, inhalation exposure to styrene at level causing maternal toxicity in the rat and up to 600 ppm in the rabbit was not associated with significant effects on the fetus. In other studies, delayed fetal development or increases in minor anomalies in rat and mouse were only observed at doses causing maternal toxicity. A range of epidemiological studies focussing on developmental effects has been conducted but most of these investigations have been too small to be conclusive. Overall, there is no evidence of an effect of styrene on human reproduction.

NATURE OF FURTHER WORK RECOMMENDED

A further *in vivo* study in a second tissue is recommended (an *in vivo* unscheduled DNA synthesis test is recommended as post-SIDS work). Consumer exposure information is needed. A national human health risk assessment is recommended to identify the need for risk reduction.

SIAM 4, 20-22 May 1996

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	**102-71-6**
Chemical Name	**Triethanolamine**
Structural Formula	**$(HOCH_2CH_2)_3N$**

CONCLUSIONS AND RECOMMENDATIONS

[x] presently of low priority for further work

[ ] requiring further information to assess identified concerns

[ ] candidate for in-depth risk assessment with a view to possible risk reduction activities

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Environment - Triethanolamine is likely to be released mainly to water, where it may biodegrade. Transfer to other environmental compartments is likely to be limited.

Triethanolamine is of low toxicity to fish, *Daphnia* and algae. Several potential release sources of triethanolamine have been identified. The PECs derived for release of triethanolamine from production are greater than the MTC and PNEC, indicating that further work may be needed to refine the assessment. The PECs derived for use of triethanolamine in metal working fluids are less than the MTC and PNEC, and indicate that triethanolamine does not pose a risk to aquatic organisms for this use.

Triethanolamine is a basic compound, thus if it is released to water in large quantities, effects on the pH of the receiving water might be expected.

Human health - Triethanolamine is of low toxicity following single exposures. There were some signs of systemic toxicity at high exposure levels, and mild skin irritation following repeated exposures using the dermal route. It is not genotoxic, carcinogenic or toxic to development or the reproductive system.

NATURE OF FURTHER WORK RECOMMENDED

No further toxicity testing is required.

Further information would help to refine the exposure assessment:

- data from production sites in other countries
- more information relating to occupational exposure and the use of triethanolamine in consumer products.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	105-99-7
Chemical Name	Dibutyl adipate
Structural Formula	$C_4H_9OOC\text{-}CH_2CH_2CH_2CH_2\text{-}COOC_4H_9$

CONCLUSIONS AND RECOMMENDATIONS

The chemical does not reveal any remarkable toxicity or ecotoxicity.

It is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Dibutyl adipate is volatile liquid and production volume is less than 100 tonnes/year in 1987 - 1992 in Japan. This chemical is used as for plasticizer for resins mainly. Dibutyl adipate is readily biodegradable. Dibutyl adipate is not hydrolyzed at pH 4, but hydrolysed at 7 and 9. The half-life is a week at pH 9. Direct photodegradation is not expected because dibutyl adipate does not absorb UV light.

The potential environmental distribution of dibutyl adipate obtained from a generic fugacity model (Mackay level III) showed the chemical will be distributed mainly to water and soil. The predicted environmental concentration (PEC_{local}) of this chemical was estimated to be 4×10^{-3} mg/l from Japanese exposure scenario.

For the environment, various NOEC and LC_{50} values were gained from test results; LC_{50} = 3.7 mg/l (acute fish); EC_{50} = 17 mg/l (acute daphnia); NOEC = 2.0 mg/l (algae); NOEC = 5.6 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to be moderately toxic to fish and daphnids and slightly toxic to algae. The lowest toxicity result for *Selenastrum capricornutum* (NOEC = 2.0 mg/l) was adopted for the calculation of a PNEC, applying an assessment factor of 100. Thus the PNEC of the chemical is 0.02 mg/l. Since the PEC is lower than the PNEC, environmental risk is presumably low.

As dibutyl adipate is produced in a closed system, exposure during synthesis may be excluded. This chemical is mainly used as a plasticizer for resins. There is a possibility of workplace exposure when the product is filled into barrels, with skin contact considered to be the main exposure route. Inhalation plays a minor role because the vapour pressure of this chemical is very low. Workers wear safety glasses and gloves during the filling process. Exposure levels calculated by the EU exposure model are 0.5 - 3.0 by inhalation and 0.1 - 1 mg/mg/m^2/day by dermal, respectively, at production site of this chemical. There are no actual measurement data of exposure. By wearing safety equipment during filling process, the exposure level can be very low.

The chemical is contained in consumer floor wax as a. Dermal exposure of this chemical is expected during housekeeping. The exposure level was estimated to be 3.6 mg/kg bw/day for one event.

For indirect exposure via the environment, the concentration in drinking water was estimated as to be less than 4×10^{-3} mg/l from the local exposure scenario.

Although the chemical showed positive result in chromosomal aberration test *in vitro* with metabolic activation, no

genotoxic effects were observed in bacteria and no chromosomal aberration were observed *in vitro* without metabolic activation. In a combined repeat dose and reproductive/developmental toxicity screening test, salivation was observed in both sexes given 1,000 mg/kg/day. No test substance-related changes were noted in body weight gains, food consumption, findings obtained from haematology testing, blood chemical examination, urinalysis and pathological examination. For reproductive/developmental end-points, there were no adverse effects of this chemical on copulation, fertility, maintenance of pregnancy, parturition and lactation. In the 1,000 mg/kg group, pup weight on day 0 and 4 of lactation was slightly lower and viability on day 4 of lactation was decreased compared to those of the control group. However, there were no malformations which were considered to be induced by this chemical. Therefore, the NOEL was 300 mg/kg/day for repeated dose toxicity as well as 300 mg/kg/day for reproductive toxicity.

For human health, margins of safety are considered to be sufficient. Therefore, health risk is presumably low.

In conclusion, no further testing is needed at present considering its toxicity and exposure levels.

NATURE OF FURTHER WORK RECOMMENDED

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	106-99-0
Chemical Name	1,3-Butadiene
Structural Formula	CH_2=CH-CH=CH_2

CONCLUSIONS AND RECOMMENDATIONS

This chemical is currently considered of low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

The total global production capacity of 1,3-butadiene is 1,202,000 - 4,960,000 tonnes/year. In Western Europe, 1,742,000 tonnes were produced in 1993 and 1,892,000 tonnes in 1994. This chemical is used as a monomer in the manufacture of a variety of synthetic rubbers and plastics (96%), or as an intermediate in the production of several other compounds (4%). Motor vehicle emissions are also a significant source of environmental exposure.

The substance is a gas, and therefore difficult to test by standard methods. No information on direct photolysis has been found, but the substance reacts rapidly in the atmosphere with hydroxyl radicals and other atmospheric oxidants. It has potential for the generation of low-level ozone and photochemical smog. No standard biodegradation tests are available, because of its high volatility. It is expected that the majority of any release will partition to the atmosphere. No measured bioconcentration factors (BCFs) are available, but low BCFs (13-19.1) have been estimated.

Few ecotoxicity data are available because of its high volatility. A 28-day NOEC for fish of 4.5 mg/l (*Brachydanio rerio, Pimephales promelas*) has been estimated using a quantitative structure-activity relationship (QSAR). No data are available for terrestrial organisms exposed via soil, but atmospheric exposure to a number of higher plants results in low toxicity. Following a detailed risk assessment in the European Union, this chemical is currently considered of low priority for further work for the environment.

1,3-Butadiene is absorbed via the lungs in animals and humans. There are no data for absorption via the oral or dermal routes of exposure, but since it is a gas it is reasonable to assume that uptake via these two routes would be minor compared with inhalation. The substance is widely distributed throughout the body. The first step in the metabolic pathway is the formation of epoxybutene. Further metabolism of epoxybutene to butenediol, diepoxybutane, and erythritol can occur. Excretion of 1,3-butadiene and its metabolites is mainly in the urine or in the breath.

This chemical is of low acute toxicity following single inhalation or oral exposure. The limited data available indicate it is of low acute toxicity to humans. The chemical does not exhibit skin irritation and there are no reports of skin or respiratory sensitisation.

Repeat-dose studies indicate the mouse to be more sensitive than the rat to 1,3-butadiene. Inhalatory repeated dose investigations in the rat produced minimal effects at 8000 ppm for 2 years. In the mouse, deaths primarily due to multi-organ tumour formation are observed at 20 ppm or above for a lifetime exposure. Additionally, in shorter-term studies in the mouse, the bone marrow has been identified as a target organ (1250 ppm).

1,3-Butadiene is genotoxic to bacterial cells *in vitro* (with metabolic activation). A number of *in vivo* studies demonstrate that it is mutagenic to somatic and germ cells in the mouse but not the rat. The metabolites epoxybutene and diepoxybutane are mutagenic in somatic cells in the mouse and/or hamster and in the germ cells of mice and rats. There is some evidence that 1,3-butadiene causes genetic damage in humans but the findings are inconsistent and overall the potential for human genotoxicity cannot be excluded.

The carcinogenicity of 1,3-butadiene has been studied in rats and mice, and there is a marked species difference in susceptibility. In the mouse, 1,3-butadiene is a multi-organ carcinogen. In the rat, the available study shows, even at high exposure concentrations, a lower tumour frequency and fewer tumour types mainly of a benign nature. The tumour types suggest hormonal influences may play a role in the rat carcinogenic response, and thus a non-genotoxic mechanism may underlie the tumour formation. It is considered that 1,3-butadiene has the potential to form genotoxic metabolites and therefore has the potential to be a genotoxic carcinogen in humans. A clear association between this chemical exposure and leukemia in humans has been demonstrated from one cohort-mortality study, with supporting evidence from a number of other studies. Thus, 1,3-butadiene may be carcinogenic in humans.

There are no adequate fertility studies available, although no evidence for an adverse effect on male fertility was seen in three dominant lethal assays in the mouse. The results of long-term toxicity and carcinogenicity studies indicate that the ovaries and testes are a target organ for 1,3-butadiene toxicity in mice (ovarian and testicular atrophy occurred at 625 and 1250 ppm in a 60-61 week repeated dose study, while malignant ovarian tumours developed in female mice exposed to 1,3-butadiene for up to 2 years). The testes are also a target organ in the rat (Leydig cell tumour formation was observed in a 2 year exposure study at 1000 and 8000 ppm). It is unclear what the effect on fertility would be from the changes that have been reported. The results of developmental studies in the rat and mouse suggest development effects are secondary to maternal toxicity and are of low concern for human health. There are no human data available for reproductive parameters.

Exposure to 1,3-butadiene is well controlled, there is only limited information regarding occupational exposure. Although this chemical is not added to consumer products, consumer exposure arises as a result of cigarette smoking (including passive smoking), and there may be exposure to residual monomer in products manufactured from synthetic polymers. Indirect exposure via the environment occurs mainly as a result of emissions from polymer production facilities.

NATURE OF FURTHER WORK RECOMMENDED

SIAM 4 agreed that the results of an ongoing epidemiology study might lead to a need for further action. Further information will be available to update the SIAR following completion of a risk assessment review within the European Union.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	107-05-1
Chemical Name	3-Chloropropene (Allylchloride)
Structural Formula	CH_2=CH-CH_2-Cl

CONCLUSIONS AND RECOMMENDATIONS

It is currently considered of low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Total European production is approximately 280000 t/a The substance is manufactured by hot chlorination (400-600^o C) of propylene. The production process is carried out in a 100% closed system. Allylchloride is predominantly (90% worldwide) used as an intermediate in the manufacture of epichlorohydrin and glycerine. It is also used as an intermediate in the production of allyl derivatives (allyl alcohol, diallyl phthalate, allylamine), in the synthesis of medical derivatives, agricultural chemicals and allyl starches, and as thermosetting resins for varnishes, plastics, and adhesives.

Most important emissions of allylchloride will probably occur to the atmosphere. Allylchloride is volatile (estimated to partition 99.35 and 0.59%, air and water respectively), will be removed rapidly from the atmosphere by photodegradation: half life for the reaction with OH-radicals is less than 1 day and if allylchloride is emitted into water it will rapidly volatilise to the air. Hydrolysis will occur (hydrolysis t ½ of 12 days, pH8), but this is not thought to be an important removal process due to the high volatilisation.

Allylchloride is considered to be toxic to fish, with 24-96 hrs LC_{50}-values ranging from 6.9 to 70 mg/l. Allylchloride is found to be also toxic to fish in a test with a deviating exposure time of 14 days. For daphnids allylchloride does not need to be classified for acute toxicity. The lowest LC_{50}-value of 0.34 mg/l is found in a 48-h study with *Xanopus laevis*. Chronic NOEC values for algae and protozoa are ranging from 6.3 to 8.6 mg/l, and for bacteria of 115 mg/l. For environmental assessment, it is decided to use the LC50 for *Xanopus laevis* to derive a PNEC (i.e. 3.4 µg/l) because clearly chronic data is not available from the most sensitive taxonomic groups.

Allychloride was found to be harmful in acute oral toxicity tests and toxic in inhalation toxicity tests. No overall NOAEL could be established from the oral studies in mice, rats and rabbits.

Inhalation studies have been carried out in mice, rats, rabbits and cats with exposures varying from 5 weeks to 6 months. The target organs were liver, kidneys and lungs and the central nervous system. In a recent adequate study, not focussing on neurotoxicity, with rats the NOAEL was 155 mg/m^3 (duration adjusted: 27 mg/m^3). At higher dose levels slight tubular degeneration in the kidneys of both sexes was observed.

The neurotoxic effects of allylchloride have been studied extensively in mice, rats, rabbits and cats. Allychloride is a neurotoxic agent, which especially damages the peripheral nervous system resulting in a dying-back pattern of axonal degeneration. In the most reliable study a NOAEL for neurotoxicity of 31 mg/m^3 (duration adjusted: 7.38 mg/m^3) has been established.

Reproduction studies have not been carried out with allylchloride. However, effects on the male reproductive system were investigated *in vitro* as well as *in vivo*. Testosterone production was not affected in rat foetal testes *in vitro*. Effects on the male gonads of rats and rabbits were observed *in vivo*. In mice, which survived a single s.c. dose ≤ 496 mg/kg b.w. allylchloride, various degrees of damage in the testes was observed. However, no histopathological effects were found in the testes of rats after subchronic inhalatory exposure to concentrations ≥ 782.5 mg/m^3. In developmental studies with rats and rabbits by the inhalation route a slight delay in skeletal development in rats was observed at maternal toxic doses. In adequately performed studies the NOAEL for foetal/embryo and maternal toxicity was 93 mg/m^3 (duration adjusted: 27.3 mg/m^3).

Based on all available mutagenicity data it can be concluded that allylchloride is mutagenic to bacteria and yeast and induces UDS in human HeLa cells, but not in embryonic testinal cells. Allychloride did not cause chromosome aberrations *in vitro* in mammalian cells. Negative results were obtained in the available *in vivo* tests.

IARC (1987) concluded that there is inadequate evidence for the carcinogenicity of allylchloride to experimental animals. Allychloride was classified in group 3.

The PEC/PNEC ratio for aquatic organism according to the USES model is 0.006 and 1.4 E-6 for the local and regional scenario, respectively, both indicating no risk for the aquatic environment.

Using the data for the Shell Pernis plant in the USES model the MOS between the overall NOAEL and the data for indirect exposure for the local scenario is 230 indicating no concern for human safety following indirect exposure.

Occupational exposure to allylchloride will occur during production, processing and transportation. For most plants workplace measurements ensure that exposure limits are below the current MAC/TLC of 3.13 mg/m^3. This value can be considered as a best worst-case Estimated Human Exposure ($EHE_{best\ worst\text{-}case}$) for production. At normal operation the Margin of Safety between the $EHE_{best\ worst\text{-}case}$ and the overall NOAEL of 31 mg/m^3 is sufficient. However, the data available for processing are insufficient to draw a firm conclusion about the Margin of Safety.

NATURE OF FURTHER WORK RECOMMENDED

Appropriate action on setting occupational exposure limits could be taken by the individual national authorities.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	108-01-0
Chemical Name	N,N-DIMETHYLAMINO-2-ETHANOL
Structural Formula	$(CH_3)_2NCH_2CH_2OH$

RECOMMENDATION OF THE SPONSOR COUNTRY

[X] presently of low priority for further work

[ ] requiring further information to assess identified concerns

[ ] candidate for in-depth risk assessment with a view to possible risk reduction activities

SHORT SUMMARY WHICH SUPPORTS THE RECOMMENDATION

Environment - Dimethylaminoethanol may be released to air and to water, where it will degrade fairly rapidly. It tends not to move from the phase to which it is released. It is of moderate toxicity to aquatic organisms; some of its toxicity may be due to changes in pH when it dissolves in water.
Estimated release to water from production via sewage treatment plant based on default values for the size of the sewage plant and the receiving river leads to concern for the aquatic environment; however dilution at actual sites is thought to be much greater, leading to no concern.

Human health - Dimethylaminoethanol is of low single exposure toxicity but has corrosive properties. It is not genotoxic or toxic to development or the reproductive system.

IF FURTHER WORK IS RECOMMENDED, SUMMARISE ITS NATURE

No further toxicity tests are required.

Information on production sites and use in corrosion inhibitor formulations would be useful to confirm the assessment. Data on these areas were requested after SIAM 3; as the subsequent information collection exercise did not produce further specific data it is not proposed to actively seek further information.

The additional exposure data provided by other Member States on the occupational and consumer end-points does not change the overall assessment of the substance as being of low risk for human health based on existing control measures.

The UK has produced a more detailed occupational risk assessment for domestic use, resulting in the following occupational exposure limits: 2 ppm 8 hour TWA and 6 ppm for a short 15 minute exposure for irritancy. Copies can be made available on request.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	112-35-6
Chemical Name	Ethanol, 2-[2-(2-methoxyethoxy)ethoxy]
Structural Formula	HO-CH_2CH_2 OCH_2CH_2OCH2CH2-OCH3

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Human Health

Ethanol, 2-[2-(2-methoxyethoxy)ethoxy] (TGME) is of low acute toxicity in experimental animals by the oral, dermal or inhalation routes of exposure. The oral and dermal LD_{50} values in rats and rabbits are 11,800 mg/kg and 7,400 mg/kg, respectively. An 8-hr exposure to a concentrated vapor of TGME resulted in no mortality in rats. Although TGME can be absorbed through the skin, acute dermal exposures generally has a minimal irritating effect. Contact with the eyes may produce mild irritation.

The repeated dose oral NOAEL of TGME in rats is 400 mg/kg/day. Systemic effects (other than male reproductive effects) noted at an oral dose of 1,200 mg/kg/day TGME for 91 days are slight hepatocellular centrilobular hypertrophy and increased relative liver weight. At 4,000 mg/kg/day TGME, 19 of 20 animals survived and the survivors exhibited reduced weight gain and food consumption, and microscopic changes in the liver (hepatocellular cytoplasmic vacuolization and/or hypertrophy and cholangiofibrosis). The severity of the lesions was minimal or mild (with the exception of moderate or marked hepatocellular cytoplasmic vacuolization in 4/15 males). In a dermal study, no systemic effects (other than male reproductive effects) were found in rats treated with up to 4,000 mg/kg/day TGME for 91 days.

Although a conventional reproductive toxicity test (i.e., mating study) with TGME has not been performed, results of existing 90-day studies that evaluated reproductive parameters indicate that TGME may cause testicular toxicity at high concentrations. Male rats orally administered 4,000 mg/kg/day TGME for 91 days exhibited testicular toxicity characterized by mild to moderate degeneration and/or minimal to moderate atrophy of the seminiferous tubules (spermatocytes or developing spermatids). In the same study, testicular toxicity was observed in 1/15 males at 1200 mg/kg/day and no testicular effects were noted at 400 mg/kg/day. Similarly, a 91-day repeated-dose dermal toxicity study in rats given 400, 1,200 or 4,000 mg TGME/kg/day showed severe testicular toxicity in 1/10 animals given 4,000 mg/kg/day and minimal decreases in developing germ cells in 1/10 rats given 1,200 mg/kg/day. No testicular effects were seen at 400 mg/kg/day. The NOAELs for reproductive toxicity determined from both the oral and dermal studies are between 400 and 1200 mg/kg/day.

Developmental toxicity experiments conducted with TGME indicate developmental effects at doses > 1,000 mg/kg/day. Effects observed in offspring from rats treated with 1,250 mg/kg/day TGME or rabbits treated with 1,500 mg/kg/day TGME during gestation included skeletal variants and decreased body weight gain.
In vitro and *in vivo* genotoxicity studies (Ames, HGPRT and micronucleus tests) with TGME were negative at concentrations up to 5,000 micrograms/plate and 5,000 mg/kg, respectively, indicating that this material is not genotoxic at these concentrations.

Environment

TGME is completely soluble in water. Its melting point is -44°C and its boiling point is 249.2°C. The vapor

pressure is < 0.01 mm Hg at 25°C and specific gravity is 1.05.

TGME released into the atmosphere will photodegrade (estimated atmospheric half life = 3.2 hr). When released to water, TGME has a low potential for bioaccumulation (estimated log K_{ow} is –1.46). Ether groups are generally stable to hydrolysis in water under neutral conditions and ambient temperatures. However, TGME will biodegrade in wastewater under aerobic conditions.

The Level III fugacity model estimated distributions of 0.0657% in air, 45.9% in water, 53.9% in soil and 0.0765% in sediment indicate a low probability of volatilization and a preference for partitioning to water and soil.
Aquatic toxicity data indicate that TGME exhibits low toxicity to aquatic species. The acute LC_{50} values for fish and Daphnia are > 10,000 mg/l. The EC_{50} for algae is > 500 mg/l and the IC_{50} for microorganisms is > 5,000 mg/l.

Exposure

In the United States, 18,000 to 25,000 tonnes of TGME are manufactured each year. TGME is produced in a closed process as a by-product from the manufacture of lighter (mono- and di-) ethylene glycol monomethyl ethers. Ninety-five percent of U.S. production is used in the formulation of hydraulic brake fluids.
Environmental releases are limited by the enclosed nature of industrial processes and the low volatility of the material. Releases are best characterized as usually occurring in very small amounts, but releases are possible wherever brakes are serviced.

The major known use of TGME is as a component of automotive brake fluids. Although exposure is limited during the formulation of TGME into brake fluids (which is done in closed systems in an industrial setting) greater exposure potential exists in automotive plants and brake service/repair shops, where brake lines and cylinders are filled with fluid, or brake systems are serviced. Exposure is more limited in automotive plants than in local shops by automated processes. Because of its low vapor pressure, inhalation exposures are expected to be insignificant. Occasional consumer exposure via brief dermal contact may occur when car owners top off their brake master cylinders from a container of fluid and possibly spill some liquid.

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION

The chemical is currently of low priority for further work due to its low hazard potential for human health and the environment.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	112-50-5
Chemical Name	Ethanol, 2-[2-(2-ethoxyethoxy)ethoxy]
Structural Formula	$HO\text{-}CH_2CH_2\ OCH_2CH_2OCH_2CH_2\text{-}OCH_2CH_3$

SUMMARY CONCLUSIONS OF THE SIAR

Analog Justification

Data for ethanol, 2-[2-(2-ethoxyethoxy)ethoxy] or triethylene glycol ethyl ether (TGEE) for some endpoints are either missing or limited. Therefore, triethylene glycol methyl ether (TGME) is used for the genetic, reproductive, neurotoxicity, and algal toxicity endpoints. Use of TGME is justified based on similar structures (i.e., the two chemicals differ by only one methylene group in the terminal alkyl moiety), as well as similarities in physicochemical and environmental fate properties and toxicity. Further, the diffusion rates through human skin are quite comparable. Finally, based on data for monoethylene glycol ethers, TGME is expected to be more toxic than TGEE, so conclusions using TGME will be more conservative.

Human Health

TGEE is of low acute toxicity in experimental animals by the oral, dermal and inhalation routes of exposure. The oral LD50 values are 8,500 and 10,600 mg/kg in male rats and all rats, respectively. In an inhalation study, a 1-hour exposure to 200 mg/L resulted in no deaths. The dermal LD50 from one study is 8,200 mg/kg. TGEE has been shown to be irritating to skin and mildly irritating to eyes of rabbits.

In a 30-day drinking water study in rats, a NOAEL of 750 mg/kg/day was identified. Changes observed at 3,300 mg/kg/day in this study were decreased weight gain, slightly increased blood urea concentrations, and "congestion and cloudy swelling of the liver (6/10) and kidney (1/10)." All animals died at 13,290 mg/kg/day. TGEE produced slight erythema and edema in rats exposed dermally at 1000 mg/kg/day for 21 days. One of five males exhibited testicular effects, which was concluded to be unrelated to treatment.

TGEE did not exhibit developmental toxicity in rats treated with up to 1,000 mg/kg/day (highest dose tested).

TGEE has not been tested for its genetic toxicity either in vivo or in vitro. Based on the lack of genotoxicity of TGME (a compound of similar structure), TGEE is not expected to be genotoxic.

Environment

TGEE is miscible (25 °C) in water and its specific gravity is 1.03 g/cm3 at 20 °C. The vapor pressure is 89.2 hPa at 20 °C. The melting point is -19°C and the boiling point is 256 °C. Due to a low calculated log Kow (-0.96), TGEE is not expected to undergo bioaccumulation in aquatic organisms.

Upon release to the atmosphere, TGEE is estimated to undergo photodegradation (atmospheric half life = 2.8 hrs). TGEE is readily biodegradable (71% after 20 days) under aerobic conditions tested in fresh water. In Level III Fugacity modeling, mass balances of < 0.001% in air, 45.3% in water, 54.6% in soil and 0.0755% in sediment were estimated and indicate a low probability of volatilization and a preference for partitioning to water and soil.

TGEE is of low acute aquatic toxicity as tested in a variety of freshwater and saltwater species. In *Pimephales*

promelas, the 96-hr LC50 is > 10,000 mg/L. In *Daphnia magna*, the 48-hr LC50 is 10,000 mg/L. In algae, the modeled LC50 (using EPIWIN) is also > 10,000 mg/L. Finally, TGEE will not adversely affect sewage treatment microorganisms (IC50 > 10,000 mg/L).

Exposure

TGEE was produced at an estimated 4,072 – 4,538 tonnes in 1990 in the U.S. TGEE is typically prepared by the reaction of ethanol and ethylene oxide in the presence of a catalyst. Approximately ninety-five percent of TGEE is used as a major raw material (diluent) in the formulation of hydraulic brake fluid.

Human exposure to TGEE may occur during manufacturing and through the use of this material in hydraulic brake fluids. Due to its low vapor pressure, inhalation exposures will be insignificant whereas dermal exposures may be higher.

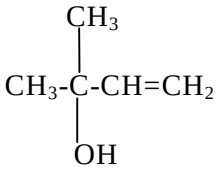
RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION

This chemical is currently of low priority for further work.

Human Health: Triethylene glycol ethyl ether possesses properties indicating a hazard for human health (dermal irritation and mild eye irritation). These hazards do not warrant further work as they are related to reversible, transient effects. They should nevertheless be noted by chemical safety professionals and users.

Environment: Triethylene glycol ethyl ether is currently of low priority for further work due to its low hazard profile.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	115-18-4
Chemical Name	2-Methyl-3-butene-2-ol
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

It is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

The production volume in Switzerland is about 10,000 tons/year. This chemical is mainly used as starting material or intermediate in the synthesis of drugs, vitamins, flavoring agents etc. Minor amounts are used as attractant in bark beetle traps. The chemical is a natural constituent of hops.

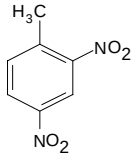
This chemical is of low acute toxicity for water organisms. It is readily biodegradable and no bioaccumulation is expected. The identified uses and the PEC/PNEC considerations derived from the available data do not indicate concern for the environment.

This chemical is of low acute toxicity and is not genotoxic. It is irritating to the eyes but not to the skin. The lowest NOAEL determined was 50mg/kg/day. Based on the available exposure information no concern for consumers and workers could be identified.

NATURE OF FURTHER WORK RECOMMENDED

No further studies are required to evaluate potential health and environmental effects.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	121-14-2
Chemical Name	2,4-Dinitrotoluene
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

The chemical is of low current priority for further work in the SIDS context

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

The production volume of 2,4-Dinitrotoluene (2,4-DNT) is ca. 140,000 t/a in Germany and ca. 264,000 in the USA. The worldwide production is estimated at ca. 850000 t/a. Nearly the entire production volume is used as intermediate in chemical synthesis. The only direct use known is as additive in explosives. 2,4-DNT can be regarded as "inherently biodegradable" with low to moderate bioaccumulation.. The most sensitive environmental species to 2,4-DNT is the crustacean *Daphnia magna* (21d-NOEC = 0.04 mg/l). The derived aquatic PNEC is 4 µg/l.

The substance is harmful with oral administration (acute LD50 = 400 - 1954 mg/kg bw). It is mutagenic in the Ames test and in in vivo tests on mammals. The NOEL for repeated dose toxicity is 0.57 - 0.71 mg/kg bw/day (2-year study). No teratogenic effects were recorded and impairment of fertility were observed at doses which also cause other effects.

The highest aquatic local PEC due to production and processing was estimated to be 1.66 µg/l in Germany and 56 µg/l for a production site in the USA. For the PEC calculation (for production and processing plants plants without exposure information), the default values defined in the EU *Technical Guidance Documents on Risk Assessment for New and Existing Substances* are used (data about the discharges via waste water are not available for production and processing plants outside of Germany). For a production plant with an unknown site location a PEC_{local} of 245 µg/l and for a processing plant a PEC_{local} of 570 µg/l is calculated.

The EHD for inhalational exposure is estimated at <0.071 mg/kg bw.

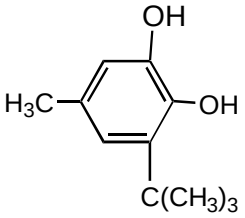
Consumer exposure is not to be expected.

In conclusion, there is currently no risk to be expected to the environment or to humans for the 3 known production and processing sites in Germany. For a known production site in the USA, 2,4-DNT represents presently a risk for the aquatic compartment. A comparison of the predicted environmental concentrations for a production and a processing site (plants without exposure information, hypothetical unknown site location with a hypothetical capacity 1000 t/a) and the predicted no-effect concentration for aquatic ecosystems indicates that a risk of damage to aquatic ecosystems is to be expected.

NATURE OF FURTHER WORK RECOMMENDED

Site specific exposure data have to be improved for all production and processing sites.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	1879-09-0
Chemical Name	2,4-Xylenol, 6-t-butyl-
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

A potential hazard to man due to a low no-effect-level in repeated dose animal studies is identified, but exposure is considered to be low.

Unless further information on exposure in other member countries presents evidence to the contrary, it is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

6-tert-Butyl-2,4-xylenol is not produced in Japan, and there are no imported volumes. However, this chemical is registered in TSCA and EINECS. This chemical is stable in acidic, neutral and alkaline solutions, and is considered as “not readily biodegradable”.

For the environment, various NOEC and LC_{50} values were gained from test results; LC_{50} = 4.4 mg/l (acute fish); EC_{50} = 5.6 mg/l (acute daphnia); EC50 = 3.6 mg/l (algae), NOEC = 1.7 mg/l (algae); NOEC = 0.32 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to be moderately toxic to fish and daphnids and algae. The lowest chronic toxicity result, 21 d-NOEC (reproduction) of *Daphnia magna* (0.32 mg/l), was adopted for the calculation of the PNEC, applying an assessment factor of 100. Thus the PNEC of 6-tert-butyl-2,4-xylenol is 0.0032 mg/l. Since the chemical is not produced in member countries, PEC/PNEC ratio could not be calculated. Therefore, it is considered to be currently of low potential risk for the environment.

The chemical showed no genotoxic effects in bacteria and in a chromosomal aberration test *in vitro*.

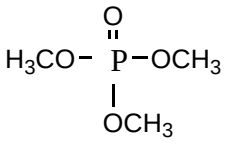
In a combined repeat dose and reproductive/developmental toxicity screening test, there were no clinical observations attributed to the administration of the test substance in parental animals. However, increases of liver and kidney weights were observed at the middle and highest dose level (30 and 150 mg/kg/day). In addition, histopathological examination showed swelling of liver cells and degeneration and protein cast of the proximal renal tubules in the groups. From the view point of reproductive/developmental end-points, only a few females at the highest dose lost their litters during lactation period. Other effects (e.g. mating, fertility and estrous cycle) were not observed. Therefore, the NOEL was 6 mg/kg/day for repeated dose toxicity and 30 mg/kg/day for reproductive toxicity.

For human health, daily intake of the chemical could not be estimated, because of the lack of exposure scenarios.

However, the health risk is presumably low due to its exposure situation.

NATURE OF FURTHER WORK RECOMMENDED

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	512-56-1
Chemical Name	Trimethyl phosphate
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

A potential hazard to man due to genotoxicity is identified, but exposure throughout OECD is low.

It is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

The production volume of trimethyl phosphate in Japan is ca. 100 - 1,000 tonnes/year in 1990 – 1993, and 500 tonnes/year in the EEC in 1987. This chemical is used as an intermediate for pesticides in closed systems or as a polymerization catalyst in industry. This chemical is stable in neutral, acidic or alkaline solutions, and is considered as “not readily biodegradable”.

The potential environmental distribution of trimethyl phosphate obtained from a generic fugacity model (Mackay level III) showed that the chemical will be distributed mainly to water and soil. Predicted environmental concentration (PEC_{local}) of this chemical was estimated to be 1.5×10^{-4} mg/l from a Japanese local exposure scenario.

For the environment, various NOEC and LC_{50} values were gained from test results; LC_{50} = > 1050 mg/l (acute fish); EC_{50} = > 1000 mg/l (acute daphnia); EC_{50} = > 1000 mg/l (acute algae); NOEC = > 1000 mg/l (algae); NOEC = 320 mg/l (long-term daphnia reproduction). The lowest chronic toxicity result, 21d-NOEC (reproduction) of *Daphnia magna* (320 mg/l), was adopted for the calculation of a PNEC. The assessment factor of 100 was used to both acute and chronic toxicity data to determine a PNEC according to the OECD Provisional Guidance for Initial Assessment of Aquatic Effects. Thus, the PNEC of the chemical is 3.2 mg/l in the present report. The PEC is lower than the PNEC, therefore the environmental risk is presumably low.

As trimethyl phosphate is produced in a closed system, exposure during synthesis may be excluded. Since this chemical is used as a polymerization catalyst, the possibility of workplace exposure through dermal route is possible when the product is filled into barrels. Dermal uptake at work place is considered to be the main exposure route while inhalation plays a minor role. Although there is no actual exposure data, using the physical-chemical properties and the EUSES model, exposure levels were calculated to be 0.5 - 3.0 mg/m^3 for inhalation and 0 - 0.1 mg/cm^2/day for the dermal route. However workers wear personal protective equipment (e.g. chemical cartridge respirator with an organic vapour cartridge) during the filling process. Therefore, the exposure at work place is considered to be very low at the present situation. Although the use and resident level of the chemical in consumer products are unknown, because it is an intermediate and under industrial use, the exposure level can also be considered to be negligible. As for indirect exposure via environment, PEC_{local} in surface water was estimated to be 1.5×10^{-4} mg/l from a local exposure scenario. The daily intake through drinking water is estimated as 5.0×10^{-6} mg/kg/day.

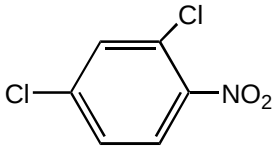
Although negative results were obtained both from an Ames test and a chromosomal aberration test *in vitro*, genotoxic effects were shown in a micronucleus test *in vivo*. In a combined repeat dose and reproductive/developmental toxicity screening test, significant decrease of body weight, significant change in haematology and clinical chemistry examines (e.g. decreased erythrocytes) were observed in parental animals. Renal toxic findings and neurotoxic effects were also seen in gross and histopathological examines (e.g. nephropathy, degeneration of nerve fibre). Increases of kidney weight were observed at the lowest dose level (40 mg/kg/day). For reproductive/developmental end-points, the fertility index and the number of implantation sites were decreased at the lowest dose. In addition, intrauterine mortality of embryos was also increased at that level. Therefore, the NOEL was less than 40 mg/kg/day both for repeated dose and reproductive toxicity.

As for indirect exposure via environment, a PEC_{local} in surface water was estimated to be 1.5×10^{-4} mg/l from local exposure scenario. The daily intake through drinking water is estimated as 5.0×10^{-6} mg/kg/day. For human health, although the NOEL is estimated to be less than 40 mg/kg/day both for repeated dose and reproductive toxicity, the margin of safety is very large. Therefore, health risk through the environment, in general, is considered to be presumably low due to its use pattern and exposure situation.

In conclusion, no further testing is needed at present considering its toxicity and exposure levels.

NATURE OF FURTHER WORK RECOMMENDED

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	611-06-3
Chemical Name	Benzene, 2,4-dichloro-1-nitro-
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

A potential hazard to the environment due to toxicity to daphnids is identified, but exposure is low in the sponsor country.

Unless further information on exposure in other Member countries presents evidence to the contrary, it is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

The production volume of 2,4-dichloronitrobenzene in Japan was less than 50 tonnes during 1990 - 1993, and 1,500 tonnes in Germany in 1990. This chemical is used as an intermediate for the synthesis of pigments, pesticides and medicinal drugs in industry in Japan. This chemical is stable in neutral, acidic or alkaline solutions, and is considered as "not readily biodegradable".

The potential environmental distribution of 2,4-dichloronitrobenzene obtained from a generic fugacity model (Mackay level III) showed that the chemical will be distributed mainly to water and soil. The predicted environmental concentration (PEC_{local}) of this chemical was estimated to be 2.7×10^{-8} mg/l from a Japanese local exposure scenario.

For the environment, various NOEC and LC_{50} values were gained from test results; LC_{50} = 13 - 21 mg/l (acute fish); EC_{50} = 12 mg/l (acute daphnia); EC_{50} = 2.0 mg/l (acute algae); NOEC = 1.8 mg/l (algae); NOEC = 0.056 mg/l (long-term daphnia reproduction). The lowest chronic toxicity result, 21d-NOEC (reproduction) of *Daphnia magna* (0.056 mg/l), was adopted for the calculation of the PNEC. The assessment factor of 100 was used to both acute and chronic toxicity data to determine PNEC according to the OECD Provisional Guidance for Initial Assessment of Aquatic Effects. Thus, the PNEC of the chemical is 0.00056 mg/l in the present report. The PEC is lower than the PNEC, therefore the environmental risk is presumably low.

2,4-Dichloronitrobenzene is produced in a closed system and is used as an intermediate in industry. As this chemical is not taken out from the vessel, the only situation that could lead to occupational exposure is when workers maintain the reaction vessel under local exhaust ventilation. Although there is no actual exposure data, using the physical-chemical properties of the substance and the EUSES model, exposure levels were calculated as 0 - 0.1 ppm for inhalation and 0 - 0.1 mg/cm^2/day for the dermal route. However workers wear personal protective equipment (e.g. chemical cartridge respirator with an organic vapour cartridge) during the filling process. Therefore, the exposure at the work place is considered to be negligible for the current situation. In addition, this chemical is not contained in consumer products, because it is an intermediate in industrial use. As for indirect exposure via the environment,

PEC_{local} in surface water was estimated to be 2.7 x 10^{-8} mg/l from a local exposure scenario. The concentration in drinking water is estimated to be less than 2.7 x 10^{-8} mg/l (corresponding to a daily dose of less that 9 x 10^{-10} mg/kg/day).

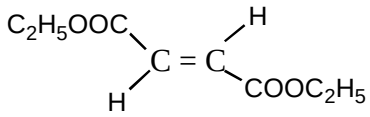
Although a positive result was obtained from an Ames test, the chemical showed no genotoxic effect in a chromosomal aberration test *in vitro*. In an OECD combined repeated dose and reproductive/developmental toxicity test, moderate effects to liver (e.g. increased liver weight and necrosis) and kidney (e.g. increased kidney weight and basophilic changes in the renal tubules) were observed at the middle dose (40 mg/kg/day). Similar slight effects to the kidney were also seen in females at the lowest dose (8 mg/kg/day). Therefore, NOEL was strictly considered to be less than 8 mg/kg/day. Regarding reproductive/developmental toxicity, the chemical did not show any effects on mating fertility or estrous cycle. However, all pups of two females were stillborn, and during the lactation period, pups of three females died at the highest dose (200 mg/kg/day). In addition, functional disturbances in delivery or lactation caused by the test substance was expected. The NOEL for reproductive toxicity was 40 mg/kg/day.

Regarding indirect exposure via environment, the daily intake through drinking water is estimated to be less than 9.0 x 10^{-10} mg/kg/day. For human health, although NOEL is estimated as less than 8 mg/kg/day for repeated dose and 40 mg/kg/day for reproductive toxicity, the margin of safety is very large. Therefore, health risk through the environment, in general, is considered to be presumably low due to its use pattern and exposure situation.

In conclusion, no further testing is needed at present considering its toxicity and exposure levels.

NATURE OF FURTHER WORK RECOMMENDED

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	623-91-6
Chemical Name	2-Butenedioic acid (E)-, diethyl ester (Diethyl fumarate)
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

A potential hazard to the environment due to moderate toxicity to fish and algae, and also a potential hazard to man due to a low no-effect-level in repeated dose animal studies are identified, but exposure is considered to be low.

Unless further information from other Member countries presents evidence to the contrary, it is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Exposure

Diethyl fumarate is not produced in Japan, and there are no imported volumes. However, this chemical is registered in TSCA and EINECS. This chemical is stable in acidic solution, but unstable in neutral (half-life: 10 days) or alkaline solutions, and is considered as “readily biodegradable”.

Environment

For the environment, various NOEC and LC_{50} values were gained from test results; 72h LC_{50} = 2.4 mg/l (acute fish); 24h EC_{50} = 11 mg/l (acute daphnia); 72h EC_{50} = 1.1 mg/l (acute algae); 72h NOEC < 0.56 mg/l (acute algae); 21d NOEC = 1.8 mg/l (long-term daphnia reproduction). As the lowest toxicity data to algae, acute-NOEC of *Selenastrum capricornutum* (0.56 mg/l) was adopted. Using an assessment factor of 100, the PNEC of the chemical is 0.0056 mg/l.

Human Health

Although positive results were obtained from a chromosomal aberration test *in vitro*, negative results were obtained in a bacterial mutation assay. In an oral combined repeated dose and reproductive/developmental toxicity test at doses of 0, 11, 30 and 100 mg/kg/day [OECD TG 422], no effects were observed on clinical signs, body weight, food consumption, urinalysis, haematology or blood chemistry examinations. Histopathological examination of the forestomach revealed thickening of the mucosal layer in both sexes of all treated groups, hyperkeratosis in males of all treated groups and in females of the 30 and 100 mg/kg groups. These changes were dose-dependent. In addition, edema in the submucosal tissue as well as ulcer and focal edema in lamina propria mucosae were noted in males and females of the 30 mg/kg groups, and vesiculation in the superficial zone of the mucosal layer was apparent in males of the 30 and 100 mg/kg groups. Absolute or relative organ weights of the kidney and liver increased in both sexes of the 100 mg/kg groups, and atrophy of the thymus was noted in females of the 30 and 100 mg/kg groups. Therefore, NOEL was considered to be less than 11 mg/kg/day. As the reproductive/developmental endpoints, no effects were

observed on the following items: reproductive ability, organ weights and histopathological appearance of the reproductive organs, parturition and maternal behavior, viability, clinical signs, body weight change and autopsy findings for offspring. Therefore, NOEL was more than 100 mg/kg/day for reproductive toxicity. For human health, NOEL is estimated as less than 11 mg/kg/day for repeated dose toxicity and 100 mg/kg/day for reproductive toxicity.

In conclusion, no further testing is needed at present considering its toxicity and exposure levels.

NATURE OF FURTHER WORK RECOMMENDED

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	67774-74-7
Chemical Name	Benzene, C10-13 Alkyl derivatives
Structural Formula	$CH_3-(CH_2)_m-CH(C_6H_5)-(CH_2)_n-CH_3$ m + n = 7 - 10

CONCLUSIONS AND RECOMMENDATIONS

It is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Benzene, C10-13 Alkyl derivatives (mixture of liner alkylbenzenes; LAB) was produced ca.230t in Italy, ca.180t in Spain, and ca.40t in Germany in 1995. LAB is almost (>99%) utilised as intermediate in the production of Linear Alkylbenzene Sulfonates (LAS). There are 3 methods of manufacturing, and all the methods are closed (reaction and transportation).

LAB is readily biodegradable. No significant direct photolysis or chemical transformation was found. Log Pow (7.5-9.12) would predict a high potential bioaccumulation in fish, but the measured BCF of 35 (*Lepomis macrochirus*) means a low bioconcentration. No significant direct photolysis or chemical transformation was indicated.

In LAB case Daphnia is recognised to be the most sensitive species on acute basis and because the BCF is low it is highly probable that Daphnia is also the most sensitive species in chronic tests.

Each PEC/PNEC ratio is under 1.

LAB produces only slight acute irritation to the skin and eye of rabbits. Only repeated doses show to give inflammatory lesions to the skin of rats. LAB does not produce sensitisation either in experimental animals or in human volunteers. There is no evidence for an accumulation in the body by intravenous, oral and dermal route in rats.

LAB assumed is rapidly and extensively eliminated principally in urine, showing only a negligible affinity to the tissues with a high lipid content or secretive actions. Moreover metabolism of the absorbed quantity is rapid and complete.

No deaths were observed in acute oral and dermal toxicity limit tests on rats and a very low inhalation toxicity was found.

Rodents exposed via inhalation to LAB for 14 weeks exhibit generally eye and nose irritation with depression of body and organ weights and elevation of hepatic enzymes in females only for the highest concentration tested.

Depressed weight gains in parental animals and in litter are observed in a two generation reproduction study on rats at highest dose. Decreases were also found in litter size, pup viability at birth, survival and weights, however no effects on fertility occurred. The significant findings only a 500mg/kg/d and the non consistent effects of treatment at lower doses show that the NOAEL for reproductive toxicity is 50mg/kg/d for both parental and neonatal animals. Ossification variation and delayed ossification are found in a developmental study, however no malformations were noted. LAB does not have any unusual or selective reproductive or developmental toxicity.

LAB is both non-mutagenic and non clastogenic, because it does not exhibit activity *in vitro* and *in vivo* test systems. LAB is clearly not classifiable as a carcinogen according to the complete carcinogenesis study.

The margins of safety range from 46 (dermal exposure) to more that 100 (inhalation exposure), so it is considered no concern for workers.

For consumers the margins of safety are very high, more than 8000, and for men exposed indirectly via the environment the margins of safety do not indicate concern ($>10^5$).

NATURE OF FURTHER WORK RECOMMENDED

No further work is recommended.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	79-01-6
Chemical Name	Trichloroethylene
Structural Formula	CCl_2=CHCl

CONCLUSIONS AND RECOMMENDATIONS

The chemical is an animal carcinogen but there was no agreement as to whether this was due to a genotoxic mechanism.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Trichloroethylene (TRI) is mostly used for metal degreasing. TRI is also used in adhesives, for consumer uses and for other uses (extraction, leather preparation, pharmaceuticals etc.).

The worst case PEC/PNEC ratios suggest that TRI is not likely to cause adverse effects in the aquatic environment. The highest $PEC_{effluent}$ (427 µg/l) is due to production of TRI, giving a PEC/PNEC ratio of 3.3 which suggests that TRI may cause adverse effects on microorganisms in a WWTP.

Within the terrestrial compartment the PEC/PNEC ratio for production is 0.48, for handling 0.5, for metal degreasing is 0.14 and for use as an intermediate is 0.12 which suggests adverse effects are unlikely to occur in soil.

TRI is likely to have little effect on stratospheric ozone and will not make significant contribution to photochemical ozone formation. However, the breakdown product, dichloroacetyl chloride may have an adverse effect upon stratospheric ozone. More information is required on the lifetime and reactions of dichloroacetyl chloride.

The main toxic effect associated with acute inhalation exposure is CNS depression. Exposure to very high concentrations causes narcosis; extensive experience in the use of TRI as an anaesthetic at concentration of 5000 to 10000 ppm has demonstrated that recovery from narcosis is usually complete. Studies in human volunteers have shown that the NOAEL for CNS depression is in the region of 300 ppm, for exposures of up to eight hours.

There are indications from human experience and studies in animals that both single and repeated dermal exposure to TRI can be irritating to the skin, as is to be expected given the defatting properties of the substance, and that it should therefore be classified as a skin irritant. Also, from the limited data which are available, it is apparent that TRI should be classified as an eye irritant.

Overall, in animals, kidney toxicity appears to be the most sensitive endpoint for both long-term repeated inhalation and oral exposure. NOAELs of 100 ppm and 50 mg/kg/day were identified in rodents for inhalation and oral exposure, respectively.

The genotoxicity of TRI has been extensively investigated in experimental test systems. TRI tested positive in a bacterial (Ames) test and a mouse lymphoma gene mutation assay, demonstrating that TRI is an *in vitro* mutagen. However, there is strong evidence that this mutagenic activity is not expressed *in vivo*.

From animal data, increased incidence of kidney and lung cancer at 100 ppm and 50 mg/kg/day were observed for inhalation and oral routes respectively. Accordingly NOAELs can be derived, although other lung changes (vacuolation of Clara cells) have been seen in mice at concentrations below 100 ppm. Since TRI does not appear to express mutagenic activity *in vivo*, it is likely that any carcinogenicity would be mediated by non-genotoxic mechanisms.

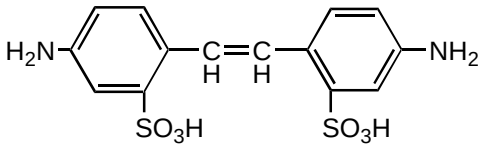
The risk of cancer under contemporary exposure condition is uncertain and therefore the exposures experienced in the workplace, in particular those encountered in poorly controlled metal cleaning operations, are of concern for human health. There are additional concerns for workers relating to repeated dose toxicity; a NOAEL for kidney of 100 ppm by inhalation having been identified from animal data.

NATURE OF FURTHER WORK RECOMMENDED

Risk management activities related to occupational exposure in the metal cleaning industry should be considered.

International consumer exposure data to be gathered.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	81-11-8
Chemical Name	Benzenesulfonic acid, 2,2-(1,2-ethenediyl)bis(5-amino-
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

The chemical does not reveal any remarkable toxicity or ecotoxicity when exposure is low.

It is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Human Health

The chemical showed no genotoxic effects in bacteria and chromosomal aberration test *in vitro*. In a NTP chronic toxicity test using rats and mice, there were no biologically significant absolute or relative organ weight, clinical pathological, or histopathological findings in rat or mice. Mean body weights were marginally decreased for high-dose male and female rats and female mice. Food consumption in dosed rats and mice was similar to food consumption in the controls throughout the studies. Survival was similar among control and treated groups of rats and mice. Ulcers of the forestomach or glandular stomach occurred in dosed rats (males: 1/50, 5/50, 4/50, females: 0/50, 1/50, 4/50). The NOEL is estimated to be less than 558 mg/kg/day in rats for repeated dose toxicity. In a combined repeat dose and reproductive/developmental toxicity screening test, parental animals exhibited no effects on reproductive parameters and there were no significant differences in number of offspring, sex ratio, etc. and no abnormal findings in the offspring. Therefore, the NOEL was estimated to be 1000 mg/kg/day for reproductive toxicity.

As for indirect exposure via the environment, PEC was estimated to be $3.7 \times 10^{-2.}$ mg/l from a local exposure scenario. Therefore, the health risk through the environment, in general, is considered to be low due to its use pattern and exposure situation.

Environment

For the environment, various NOEC and LC_{50} values were gained from test results; LC_{50} = > 1000 mg/l (acute fish); EC_{50} = 210 mg/l (acute daphnia); EC_{50} = 76 mg/l (acute algae); NOEC = 32 mg/l (algae); NOEC = 37 mg/l (long-term daphnia reproduction). The lowest toxicity result (72h-NOEC, biomass, for *Selenastrum capricornutum*, 32 mg/l) was used to derive a PNEC. An assessment factor of 100 was used according to the OECD Provisional Guidance for Initial Assessment of Aquatic Effects. Thus, PNEC of the chemical is 0.32 mg/l in the present report. The PEC is lower than the PNEC. The environmental risk is presumed to be low.

Exposure

Production and import volumes of 4,4'-diamino-2,2'-stilbenedisulfonic acid (DSSA) in Japan is ca. 1,000 and 35-77 tonnes/year, respectively, in 1988-92. Production volume is 10,000 tonnes/year in Germany. This chemical is used as an intermediate for pigments and fluorescent brighteners in closed systems in Japan. This chemical is stable in neutral, acidic or alkaline solutions, and is considered to be "not readily biodegradable". Direct photodegradation is expected as this chemical absorbs UV light with half-life of about one week.

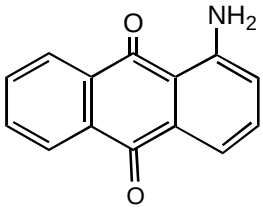
PEC_{local} have been calculated based on an emission and effluent scenario and a dilution factor. PEC_{local} for the aquatic compartment was 3.7×10^{-2} mg/l.

As DSSA is produced in a closed system, exposure during synthesis may be excluded. Workplace exposure through the inhalation route is possible when the raw materials are cast into vessels. However workers wear personal protective equipment (e.g. safety glasses, dust respirator, rubber gloves) during the filling process. Therefore, the exposure at the workplace is considered to be negligible. In addition, DSSA is not contained in consumer products, because it is an intermediate for industrial use.

NATURE OF FURTHER WORK RECOMMENDED

No further testing is needed at present considering its toxicity and exposure levels.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	82-45-1
Chemical Name	9,10-Anthracenedione, 1-amino-
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

A potential hazard to the environment due to toxicity to algae is identified, but exposure is low in the sponsor country.

Unless further information on exposure in other Member countries presents evidence to the contrary, it is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Production volume of 1-aminoanthraquinone in Japan is ca. 1,000 - 2,000 tonnes/year in 1990-1993. This chemical is used as intermediates for dyes and pharmaceuticals in closed system in Japan. This chemical is stable in neutral, acidic or alkaline solutions, and is considered as “not readily biodegradable”. Direct photodegradation is expected as this chemical absorbs UV light with half-life of about one week.

The potential environmental distribution of the chemical obtained from a generic fugacity model (Mackey level III) showed that the chemical would be distributed mainly to water and soil. Predicted environmental concentration (PEC_{local}) of this chemical was estimated as 1.7×10^{-4} mg/l from Japanese local exposure scenario. As indirect exposure, the daily intake through drinking water is estimated as 5.6×10^{-6} mg/kg/day and through fish is calculated as 3.5×10^{-2} mg/kg/day.

For the environment, various NOEC and LC_{50} values were gained from test results; LC_{50} = > 1000 mg/l (acute fish); EC_{50} = > 1000 mg/l (acute daphnia); EC_{50} = 0.25 mg/l (acute algae); NOEC = 0.10 mg/l (acute algae); NOEC = 0.32 mg/l (long-term daphnia reproduction). From the lowest toxicity data to algae, acute-NOEC of *Algae* (0.1 mg/l) was adopted for the calculation of PNEC. The assessment factor of 100 was used to both acute and chronic toxicity data to determine PNEC according to the OECD Provisional Guidance for Initial Assessment of Aquatic Effects. Thus, PNEC of the chemical is 0.001 mg/l in the present report. The PEC is lower than the PNEC, therefore environmental risk is presumably low.

As 1-aminoanthraquinone is produced in a closed system, exposure during synthesis may be excluded. The product is filled into barrels under the local exhaust ventilation. Inhalation at work place is considered to be main exposure route while skin contact plays a minor role. However workers wear personal protective equipment (e.g. safety glasses, dust respirator, rubber gloves) during the filling process. Therefore, the exposure at work place is considered to be negligible at present situation. In addition, this chemical is not contained in consumer products, because it is an intermediate in industrial use.

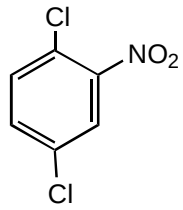
Although the chemical showed positive results only in *S. typhimurium* TA 1537 with metabolic activation, negative results were obtained by other bacterial strains and chromosomal aberration test *in vitro*. In a combined repeat dose and reproductive/developmental toxicity screening test, several toxicological findings in kidney and spleen were observed at the lowest dose (eosinophilic droplet/body [kidney], nephropathy [spleen]). The parental animals exhibited no effects on reproductive parameters such as fertility index. However, nursing behaviour disappeared in all of the treatment female groups. Viability of pups on day 4 after birth was decreased in all treatment groups. Therefore, NOEL was less than 40 mg/kg/day both for repeated dose toxicity and reproductive toxicity.

As for indirect exposure via environment, PEC was estimated as $1.7 \times 10^{-4.}$ mg/l from local exposure scenario. The daily intake through drinking water is estimated as 5.6×10^{-6} mg/kg/day and through fish is calculated as 3.5×10^{-3} mg/kg/day. For human health, although NOEL is estimated as less than 40 mg/kg/day for both repeated dose and reproductive toxicity, the margin of safety is large. Therefore, health risk through the environment, in general, is considered to be presumably low due to its use pattern and exposure situation.

In conclusion, no further testing is needed at present considering its toxicity and exposure levels.

NATURE OF FURTHER WORK RECOMMENDED

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	89-61-2
Chemical Name	Benzene, 1,4-dichloro-2-nitro- (2,5-Dichloronitrobenzene)
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

A potential hazard to man due to genotoxicity is identified, but exposure is low in the sponsor country.

Unless further information on exposure in other Member countries presents evidence to the contrary, it is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Exposure

The production volume of 2,5-dichloronitrobenzene in Japan was ca. 200 - 1,200 tonnes/year in 1988 – 1992, and 2,400 - 2,800 tonnes/year in Germany. This chemical is used as an intermediate for pigments, pesticides and UV absorbents in closed systems in Japan. This chemical is stable in neutral, acidic or alkaline solutions, and is considered as “not readily biodegradable”.

The potential environmental distribution of the chemical obtained from a generic fugacity model (Mackey level III) showed that the chemical would be distributed mainly to water and soil. The Predicted Environmental Concentration (PEC_{local}) of this chemical was estimated as 8.0×10^{-4} mg/l in a Japanese local exposure scenario

As 2,5-dichloronitrobenzene is produced in a closed system, exposure during synthesis may be excluded. Workers wear personal protective equipment (e.g. a chemical cartridge respirator with an organic vapour cartridge) when filling barrels with the product. Therefore, the exposure in the workplace is considered to be negligible in the present situation. In addition, this chemical is not contained in consumer products, because it is an intermediate in industrial use. As for indirect exposure via the environment, the daily intake through drinking water is estimated to be 2.6×10^{-5} mg/kg/day and through fish is calculated as 1.2×10^{-3} mg/kg/day.

Environment

For the environment, various NOEC and LC_{50} values were gained from test results; 96h-LC_{50} = 5.4 - 8.5 mg/l (acute fish); 24h-EC_{50} = 8.0 mg/l (acute daphnia); 72h-EC_{50} = 5.0 mg/l (acute algae); 72h-NOEC = 2.0 mg/l (algae); 21d-NOEC = 1.0 mg/l (long-term daphnia reproduction). The lowest chronic toxicity result for daphnia [21d-NOEC (reproduction) of *Daphnia magna* (1.0 mg/l)] was used with an assessment factor of 100 to determine the PNEC

according to the OECD Provisional Guidance for Initial Assessment of Aquatic Effects. Thus, the PNEC of the chemical is 0.01 mg/l. The PEC is lower than the PNEC. The environmental risk is presumed to be low.

Human Health

The chemical showed genotoxic effects in the Ames test and the chromosomal aberration test *in vitro*. In a repeated dose toxicity test, a slight effect to the liver (e.g. increased liver weight) and damage in the reproductive system (e.g. necrosis of germ epithelium, azoospermia) were observed. The NOEL was 10 mg/kg/day. In a preliminary reproductive/ developmental screening toxicity test, one dam, receiving 60 mg/kg/day, delivered dead pups. In the highest dose group (200 mg/kg/day), one dam died on day 20 of the pregnancy, one during the delivery period and four during the lactation period. A lack of care behaviour was also found in dams at the highest dose level. At that level, many pups died during the lactation period and a reduced body weight of the pups was observed. In this study, suppression of body weight gains and food consumption and an effect to the testes were also observed in adult rats at the highest dose. The NOEL for reproductive toxicity was 20 mg/kg/day.

For human health, the NOEL is estimated as 10 mg/kg/day for repeated dose and 20 mg/kg/day for reproductive toxicity. As for indirect exposure via the environment, the PEC was estimated as 8.0×10^{-4} mg/l in a local exposure scenario. The daily intake through drinking water is estimated as 2.6×10^{-5} mg/kg/day and through fish is calculated as 1.2×10^{-3} mg/kg/day. The margin of safety is large. Therefore, the health risk through the environment, in general, is considered to be low due to its use pattern and exposure.

In conclusion, no further testing is needed at present considering its toxicity and exposure levels.

NATURE OF FURTHER WORK RECOMMENDED

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	107-64-2
Chemical Name	Dioctadecyldimethylammonium chloride
Structural Formula	$(n\text{-}C_{18}H_{37})_2N^+(CH_3)_2Cl^-$

CONCLUSIONS AND RECOMMENDATIONS

The substance is currently of low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Exposure

Dimethyldioctadecylammonium chloride (DODMAC) as an isolated substance is not produced or used in a commercial range. DODMAC is the major component in the technical product ditallowdimethylammonium chloride (DHTDMAC). The alkyl chains of this compound consist of 60-70% C18-chains, so the proportion of DODMAC is about 42% related to the total content of dialkyldimethylammonium compounds. The actual production volume was estimated at 5,004 t in 1996 and 5,651 t in 1997. DHTDMAC is used as fabric softener, as additive in car washing agents and cosmetics, to activate organic clays (bentonites), in sugar refining, as anti-static and disinfection agent, corrosion inhibitor and wood impregnation. The use of DHTDMAC as fabric softener has been strongly diminished in the last years in several EU countries. Releases of DODMAC into the environment occur during production, processing to and use of activated bentonites and due to the use as fabric softener and in hair conditioners and car washing agents via household sewage. Exposure of the terrestrial compartment is expected due to sludge application. DODMAC has been detected in drinking water received from bank filtrate and surface water.

Hazards to the Environment

DODMAC is not readily biodegradable. Its removal in wwtps (ca. 95%) is mainly due to ad-sorption onto sludge. For the degradation in soil and sediment a half-life of 500 d resp. 5000 d was derived. Based on the molecular structure, no abiotic degradation (e.g. hydrolysis, photolysis) under environmental conditions is expected.

No data for the vapour pressure are available. Based on the molecular structure, no volatility is expected.

Both DODMAC and DHTDMAC have to be considered as nearly insoluble in water.

However, the compounds form stable dispersions in water containing unilamellar or multilamellar particles such as vesicles. Both substances can also form mixed aggregates with other substances, e.g. anionic tensides or humic substances. DODMAC adsorbs onto both the mineral and the organic fraction of soil and sediments. For the assessment, a value of 10,000 l/kg dw is used for both Kp_{sed} and Kp_{soil}.and of 16,800 l/kg dw for Kp_{susp}.

From a bioaccumulation study with fish a BCF of 13 was derived. For the sediment-dwelling organisms *Lumbriculus variegatus* a BSAF (biota sediment accumulation factors) of 0.28 was found and for *Tubifex tubifex* a value of 0.78. From these values it can be concluded that DODMAC has a low bioaccumulation potential.

Short- and long-term tests are available with fish, invertebrates and algae using both laboratory water and river water. As it is assumed that tests with river water are more relevant these values are used for the environmental hazard assessment.

The most sensitive aquatic species to DODMAC is the algae *Selenastrum capricornutum*: in river water tests, a 5d-NOEC = 62 µg/l was determined, while in laboratory water, the 96 h-NOEC was 6 µg/l. From a long-term test with *Daphnia magna* a 21d-NOEC for reproduction of 380 µg/l in river water was derived. In an embryo-larval test with *Pimephales promelas* a 33d-NOEC of 230 µg/l in river water was found. With an assessment factor of 10 a $PNEC_{riverwater}$ of 6.2 µg/l was derived from the NOEC for Selenastrum capricornutum.

In long-term tests with sediment organisms the following effect values were obtained:

Chironomus riparius: 24d-NOEC = 876 mg/kg dw
Lumbriculus variegatus: 28d-NOEC = 5000 mg/kg dw
Tubifex tubifex: 28d-NOEC = 1515 mg/kg dw; 28d-EC_{10} = 550 mg/kg dw
Caenorhabditis elegans: 72h-NOEC = 1350 mg/kg dw

A PNECsed of 55 mg/kg dw was derived from the EC_{10} for *Tubifex* using an assessment factor of 10.

From effect values with terrestrial organisms a PNECsoil of 20 mg/kg was derived.

Human Health

Human data on the acute toxicity and on local irritation/corrosion caused by DODMAC are not available. In rats, the substance exhibited only low acute toxicity with oral LD_{50} > 2000 mg/kg bw, dermal LD_{50} > 200 mg/kg bw and inhalation LC_{50} > 180 mg/l/1 hour.

Pure DODMAC causes serious damage to the eyes but only moderate irritation to the skin of rabbits. Data on respiratory irritation is not available. Technical grade DODMAC, however, has proven to be corrosive to the skin of rabbits because of a high content of isopropanol.

DODMAC enhances the allergic potency of other chemical substances, but does not seem to cause skin sensitization by itself as judged on the basis of tests with relevant concentrations of DODMAC.

There is no information on health effects in humans following repeated exposure to DODMAC via any route. Following repeated oral exposure of 500 mg/kg bw/d of DODMAC to rats degeneration of adrenal cortex was induced. Comparable lesions in the adrenals were also seen after 500 mg/kg bw/d DHTDMAC, additional effects were reticuloendothelial hyperplasia and accumulation of foamy macrophages of mesenteric lymph nodes and increased incidence of chronic liver inflammation. No adverse effects were reported up to 100 mg/kg bw/d DODMAC (NOAEL). After repeated dermal application to rabbits, local irritation but no systemic toxic effects were observed up to 40 mg/kg bw/d (NOAEL). A systemic LOAEL was not determined. There is no information on effects after prolonged inhalation exposure to rodents.

DODMAC showed negative results in bacterial mutation tests and in an *in vitro* chromosomal aberration test. There is no evidence of a genotoxic potential of the substance. No data is available on carcinogenic effects of DODMAC or DHTDMAC. There are no data from mutagenicity studies which give concern regarding carcinogenicity of both substances.

There is no human data on the reproductive toxicity of DODMAC. In an oral study on rats according to OECD Guideline 421 a dose of 500 mg/kg bw/d led to impaired reproductive performance in combination with clear signs of general toxicity. Based on the reduced mating, fertility and gestation indices a NOAEL for reproductive toxicity of 125 mg/kg/d can be estimated.

No specific human population at risk could be identified within the general population.

NATURE OF FURTHER WORK RECOMMENDED

This substance has been agreed in the European Union Risk Assessment Program under Regulation EEC/793/93 with the following conclusion: There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	112-34-5
Chemical Name	2-(2-Butoxyethoxy)ethanol
Structural Formula	CH3(CH2)3-O-CH2CH2-O-CH2CH2-OH

CONCLUSIONS AND RECOMMENDATIONS

It is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

2-(2-Butoxyethoxy)ethanol (DEGBE) is mainly used as solvents. During 1991-1993 the annual production of DEGBE in EU ranged from 20,000 to 80,000 tonnes (IUCLID). DEGBE has a wide range of uses as a (co)solvent with applications in paints, dyes, inks, detergents and cleaners. The major function of this agent is to dissolve various components of mixtures in both aqueous and non-aqueous systems.

DEGBE may be released into the environment during its production and other life cycle steps. DEGBE can be regarded as readily biodegradable. Volatilization of DEGBE from surface waters and moist soil is expected to be very low. Based on Kp(0.03l/kg) is expected to be highly mobile in soil. From the BCF calculated from logKow, DEGBE is expected to have a low bioaccumulating potential in the environment.

LC50 for short term toxicity to fish is 1150mg/l(7d; *Poecilia reticulata*), EC50 for short term toxicity to daphnids is 2850mg/l (24h; *Daphnia magna*), NOEC for algae toxicity data is 53mg/l(8d; *Microcystis aeruginosa*). PNEC for aquatic is 1mg/l, for micro-organisms is 71mg/l, for terrestrial is 0.14mg/l. (derived, no data available).

DEGBE has a low acute toxicity by oral and dermal routes. DEGBE should be classified as irritant to eyes, but not as irritant to the skin. DEGBE should not be classified as sensitizing to the skin. For the repeated dose toxicity (inhalation study), there found local lung effects, and liver effects, the NOAEL was considering 94mg/m3. In oral studies, DEGBE caused effects in liver, spleen, kidneys and haemotological parameters. For risk assessment it should be weighed that effects were observed in females in the 13-weeks study (51 and 254mg/kg), and only males were tested in the 6-weeks study. The dermal NOAEL for DEGBE is considered to be 2000mg/kg bw/d, and it caused no systemic effects in rats.

For genotoxicity, DEGBE is not mutagenic. No carcinogenicity studies are available.

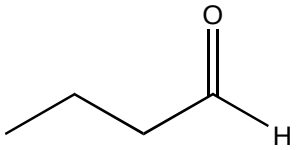
In a one-generation gavage study with rats the NOAEL for fertility was 1000mg/kg bw/d. as for developmental effects the oral NOAEL was established at 500mg/kg bw/d. The only effect observed at the next higher dose level tested was reduced body weight gain of the pups. DEGBE caused no teratogenic effects after oral administration. No effects were observed in a dermal one-generation study at doses up to 2000mg/kg bw/d.

For risk assessment, health risks for the consumer are expected to occur due to the use of DEGBE in paints. From the occupational exposure, there is a need for limiting the risks.

NATURE OF FURTHER WORK RECOMMENDED

Although a concern for consumer exposure through its use in paint was identified, additional information from the US may modify the conclusion derived from modelling.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	123-72-8
Chemical Name	Butyraldehyde
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

The chemical is currently considered of low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Butyraldehyde is a water-white organic liquid with very low odor threshold and flash point, and relatively high water solubility. The estimated annual production of butyraldehyde in the United States is on the order of 600,000 to 900,000 metric tonnes, and it is used extensively as an intermediate. Production of butyraldehyde and conversion to other chemicals take place in closed systems because of the volatile nature of this chemical. More than 90 % of all butyraldehyde produced is consumed on-site, and the remainder is sold to domestic customers who then consume it during synthetic processes. Less than 0.05 % is lost to the environment.

U.S. EPA toxic Release inventory figures indicate that, because of its volatility, virtually all of the butyraldehyde released goes into the air. Butyraldehyde undergoes photolysis in air, and in biodegradable in water and soil, both aerobically and anaerobically. Computer modeling and actual tests indicate that butyraldehyde is substantially removed from the atmosphere by photolysis and reaction with hydroxy radicals. The small amount that does remain in water or soil is degraded both aerobically and anaerobically. Limited monitoring for butyraldehyde in surface waters confirms this with concentration values ranging from 6 to 15 µg/L. Monitoring in ambient air beyond facility sites indicates levels typically below 1 ppb.

Butyraldehyde has been tested for aquatic toxicity in daphnia, 3 fish species, 2 algae species, 3 protozoan species, and 2 bacterial species. The range of EC_{50}s was from 13.7 to 195 mg/L, and the range of MICs was from 4.2 to 100 mg/L. Based on its estimated bioconcentration factor of 3, it is not likely that butyraldehyde would bioaccumulate. No data were found regarding toxicity to plants or other terrestrial organisms, but soil levels of butyraldehyde are expected to be negligible due to high volatility and rapid degradation. Butyraldehyde may be considered to be moderately toxic to aquatic organisms, however, virtually all of the butyraldehyde released into the environment goes into the air.

Occupational exposure is expected to be low since production of butyraldehyde and conversion to other chemicals takes place in closed systems. Workplace exposure levels are typically below 1 mg/L on an 8-hour time-weighted-average. This chemical is not present in consumer products, therefore there is no expected consumer exposure.

Most of the identified hazards are associated with butyraldehyde's irritant properties. Solvents are known to cause irritation by defatting and drying of tissues. No specific target organs or toxic endpoints were identified in repeated dose studies. Butyraldehyde was negative in the Ames test, negative for chromosome aberrations in human

lymphocytes, but male Q strain mice showed evidence of chromosome damage during spermatogenesis. These equivocal results fail to implicate butyraldehyde as a specific mutagenic chemical. Although no data were available on reproductive and developmental toxicity test, it is unlikely that butyraldehyde would be a specific reproductive or developmental toxin under realistic conditions because its irritant properties limit exposure, and its chemical reactivity further restricts it from reaching specialized reproductive or developmental target tissues in substantial amounts.

NATURE OF FURTHER WORK RECOMMENDED

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	127-18-4
Chemical Name	Tetrachloroethylene
Structural Formula	$Cl_2C=CCl_2$

CONCLUSIONS AND RECOMMENDATIONS

The chemical is a candidate for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

The major uses of tetrachloroethylene are as a dry cleaning solvent and a chemical intermediate. It is also used in metal degreasing and extraction processes. Some minor uses have been reported, which include use as a textile scouring solvent, fumigant, stain remover, paint remover and heat transfer media ingredient.

Tetrachloroethylene is distributed between environmental compartments by a number of different process. These include volatilisation, precipitation and adsorption, the processes responsible being dependent upon the nature of the release. Based upon its environmental chemistry, computer models predict that the atmosphere will be the major sink for tetrachloroethylene.

For the environment, various PNEC values were derived from test results (51 µg/l for water, 100 mg/l for microorganisms in WWTP, 632 µg/kg for sediment, 0.1 mg/kg for terrestrial organisms). Most of PEC/PNEC ratios are lower than 1, however, in the worst case scenario prediction for the aquatic compartment a PEC/PNEC ratio higher than 1 is obtained. As this calculated PEC uses worst case assumptions it is likely that actual concentrations are lower than this. If the water quality objective of 10 µg/l is applied for tetrachloroethylene releases, future concentrations of tetrachloroethylene in surface water should not exceed 10 µg/l, at this level the PEC/PNEC ratio is less than 1. In the terrestrial compartment a $PEC:PNEC_{local}$ >3 is achieved, however, tetrachloroethylene is very volatile and if applied to soil would be expected to evaporate rapidly from the soil surface. A low K_{oc} indicates the bioaccumulation and biomagnification potential of tetrachloroethylene is low. (This is supported by reported data.)

Studies in experimental animals and humans have shown that tetrachloroethylene is rapidly and extensively absorbed following inhalation and oral exposure; the rate of skin penetration appears to be lower than for some other solvents. The main toxic effect associated with acute inhalation exposure is CNS depression, and accidental exposure to very high concentrations has led to narcosis, unconsciousness and even death. Human experience and/or animal data indicate that tetrachloroethylene is irritating to the skin and to the respiratory tract.

Tetrachloroethylene is clearly carcinogenic in standard animal studies, producing liver tumours in mice and kidney tumours in rats. However, consideration of the mechanisms underlying the appearance of these tumours indicates that they are highly unlikely to be of any significance in relation to human health. There is no convincing evidence for any increased risk of cancer in humans resulting from exposure to tetrachloroethylene.

The majority of measurements of worker exposure to airborne tetrachloroethylene in manufacturing were low, with significant excursions which would be controlled by the use of respiratory protective equipment. Inhalation exposures for recycling and use as a chemical feedstock were similarly low, although based on very little

information. Inhalation exposures in dry-cleaning and metal degreasing were somewhat higher. Under certain circumstances there may be additional exposure via the dermal route, although this may be readily controlled with appropriate protective clothing.

Consumer exposure to tetrachloroethylene is restricted to contact following dry-cleaning of clothes and other articles. Exposure falls into two distinct categories; those from contact with professionally dry-cleaned items and those arising from the use of coin-operated dry-cleaning machines. Whilst the former category does not give grounds of concern in relation to human health, the use (and foreseeable misuse) of coin operated machines has resulted in evidence of central nervous system depression, including one reported fatality.

NATURE OF FURTHER WORK RECOMMENDED

A retrospective epidemiological study on the risk of spontaneous abortion in dry-cleaning workers is needed (currently being carried out).

There is a need for limiting the risks for consumers on the use (and foreseeable misuse) of coin-operated dry-cleaning machines

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	151-21-3
Chemical Name	Sodium dodecyl sulfate (SDS)
Structural Formula	CH_3-$(CH_2)_{11}$-O-$SO_3^-Na^+$

RECOMMENDATION OF THE SPONSOR COUNTRY

Based on an initial assessment of the effect and exposure data provided in the SIDS dossier, the chemical can be considered to present a low potential for risk to man and the environment. Thus there is no current priority for undertaking post-SIDS testing and/or exposure analysis or an in-depth assessment.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

The production volume of SDS is ca. 10,000 t/a in Germany. SDS is used as a surfactant in detergents, dispersants, cosmetics and toiletry. SDS is classified as "readily biodegradable" with "low bioaccumulation". The most sensitive environmental species to SDS is the clam *Corbicula fluminea* (30d-NOEC = 0.65 mg/l).
All relevant toxicity endpoints are covered. SDS is a substance of low toxicity. The substance did not induce mutations in different test systems. The lowest NOAEL was established for repeated dose toxicity, being 100 mg/kg bw/day.

The aquatic local PEC was estimated to be 2.3 µg/l, additional to a "background" regional PEC of further 2.3 µg/l.
It is calculated that adult consumers may be exposed to up to 0.030 mg/kd/day and that babies may be exposed to 0.034 mg/kg/day. The highest consumer exposure, however, is estimated to occur to children, with the ***worst case*** exposure being 0.160 mg/kg/day. Babies (ca. 0.25 mg/kg/day) and adults (ca. 0.05 mg/kg/day) are exposed to a lesser extent. Occupational exposure is calculated to be about 0.100 mg/kg/day, and the combined consumer and occupational exposure for workers is about 0.130 mg/kg/day.

Based on the NOEC of 0.65 mg/l, a risk to the aquatic compartment is not to be expected.
A safety margin for ***worst case*** human exposure (children) of > 600 was established in the risk assessment. Taking into account the quality and quantity of the toxicological data and the kind of health effects observed (mild hepatotoxicity), a safety margin of > 600 is considered sufficient. Therefore, it is concluded that sodium dodecyl sulfate is of no concern with respect to human health.

NATURE OF FURTHER WORK RECOMMENDED

none

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	76-03-9
Chemical Name	Trichloroacetic acid
Structural Formula	CCl_3-COOH

CONCLUSIONS AND RECOMMENDATIONS

Environment: A potential risk to the aquatic compartment is identified due to high toxicity to algae and local exposure from use as auxiliary in textile dyes, waste water from electroplating facilities, textile washing and pulp mills. A potential risk to the terrestrial environment is identified due to high toxicity to plants and global exposure from the decomposition of C2-chlorocarbons.

Human Health: The chemical is reprotoxic, corrosive and an eye irritant but adequate protection measures are currently being applied. Trichloroacetic acid is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

The production volume of trichloroacetic acid (TCA) is ca. 1000 t/a in Germany. TCA is mostly used in the production of TCA Na-salt used as a herbicide. TCA is also used as an auxiliary in textile dying processes.

TCA is stable in neutral solution and is classified as "non biodegradable" with a "low bioaccumulation potential" for fish and a "high bioaccumulation potential" for terrestrial plants. The most sensitive environmental species to TCA is the alga *Chlorella pyrenoidosa* (14d-NOEC = 0.01 mg/l) and pine (60d-EC10 = 0.12 mg/kg).

The acute oral, dermal and inhalation toxicity is low. This chemical is corrosive and strongly irritant to the eyes. The NOEL in a 90-day study in dogs - the most sensitive species tested - was determined as 500 ppm (approx. 30 mg/kg bw/day). The NOEL for repeated dose toxicity in a 4-month feeding study with rats was 4000 ppm (365 mg/kg bw/day), the NOEL in a 2-year feeding study in rats was 1600 ppm (80 mg/kg bw/day).

An inconsistent picture was found in tests on genotoxic action. Point-mutation tests were predominantly negative. *In vivo* tests of chromosome mutations were mostly positive, but effects only appeared after high loading of the animals. The SCE test in mice was negative. The results of a micronucleus test in mice are apparently not reproducible. The end point of the sperm anomaly test is not necessarily due to genetic damage. The validity of the positive test results described for the clastogenic effects in mice suffers from the partly insufficient experimental procedure.

Drinking water studies in male and female mice to 52 or 61 weeks gave an increased incidence of tumours in the livers of the male mice only. A 2-year feeding study with rats and a drinking water study over 100 - 104 weeks in rats showed no evidence of carcinogenicity.

Reproduction toxicology investigations in rats showed maternal and embryonic toxicity from 330 mg/kg bodyweight and from 800 mg/kg also embryo-lethality. In all dose-groups there was a dose-dependent increase in visceral anomalies, particularly in the cardiovascular system. The mean frequency of soft tissue malformations ranged from

9% at the low dose (330 mg/kg) to 97% at the high dose (1800 mg/kg/day). A NOAEL could not be established. Based on these findings TCA was considered to be developmentally toxic in the pregnant rat at doses of 330 mg/kg and above.

The aquatic local PEC probably due to its use in textile finishing industry was estimated to be 7 - 27 µg/l. The PEC in natural soil due to atmospheric oxidation of C2-chlorocarbons is 8 - 150 µg/kg.

In conclusion, TCA represents a risk to both the hydrosphere as well as the soil compartment.

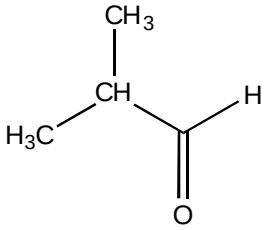
Considering the low exposure potential to humans, available toxicity data support a low risk to human health. The tumorigenic action in male mouse liver corresponds to the type, which leads to liver tumours preferentially in male mice via peroxisome proliferation, hepatotoxicity and liver cell proliferation.

NATURE OF FURTHER WORK RECOMMENDED

There is a need for consideration of risk management measures, concerning the environment and these should be addressed by the Risk Management Advisory Group.

Measurements in forest soils should be performed to actualise the soil pollution.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	78-84-2
Chemical Name	Isobutanal
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Analog justification

Based on structure-activity considerations, data on the isobutanal analogs butyraldehyde (CAS No. 123-72-8), propionaldehyde (CAS No. 123-38-6) and isovaleraldehyde (CAS No. 590-86-3) were incorporated into the SIAR and SIDS Dossier to provide a more complete evaluation of the toxicity of isobutanal.

Human Health

Studies have been conducted that identify tissues and organs most sensitive to the effects of isobutanal. Direct contact produced an irritant response, and repeated inhalation exposure to 500 ppm and higher can lead to lesions of the tissues of the nasal mucosa. A developmental toxicity study indicated that isobutanal does not pose a hazard to developing fetuses at exposure concentrations up to 4000 ppm. Effects on male reproductive organs occurred at 4000 ppm and were accompanied by significant toxicity and mortality. Sperm motility after repeated exposure to rats was significantly decreased at 500 and 1000 ppm but was comparable to the controls at 2000 and 4000 ppm, with an overall conclusion that the effect of isobutanal on sperm motility was negative. There is *in vitro* and *in vivo* evidence that isobutanal causes mutagenic and genotoxic effects in mammalian cells. NTP carcinogenicity studies in rats and mice did not reveal any carcinogenic activity for isobutanal.

Environment

Isobutanal is a liquid at ambient temperatures with a melting point of -66 ^{o}C. It is soluble in water (25 g/L at 20 ^{o}C, 89 g/L at 25 ^{o}C), has a high vapor pressure (18.4 kPa at 20 ^{o}C; 172 mm Hg or 22.9 kPa at 25 ^{o}C) and a low octanol water partition coefficient (Log Kow = 0.77 at 25 ^{o}C). Isobutanal oxidizes slowly upon exposure to air, forming isobutyric acid; peroxides or peracids may also form. It is considered a highly flammable liquid which can easily be ignited by heat, sparks or flame. Its flashpoint is less than –18 ^{o}C. The flammability limits are 1.6% (lower) to 10.6% (upper).

Based on Level III distribution modeling, the majority of isobutanal released into the environment would partition into the water (64.8%), soil (27.4%) and air (7.72%). Measured and calculated concentrations in surface waters are below prediced no-effect concentrations. Modeling predicts that isobutanal is biodegradable and is not expected to accumulate in the environment.

For isobutanal, a static test with fathead minnows (P*imephales promelas*) was reported to give a 96-hour LC_{50} of

23 mg/L. With *Daphnia magna* Strauss, the reported 48 h EC_{50} was 277 mg/L. The isobutanal toxicity to algae was tested with *Scenedesmus subspicatus* to give a 72-hour LC_{50} of 84 mg/L.

Exposure

The worldwide production of isobutanal in 1993 *ca*.700 807 metric tonnes (1545 million pounds);of this, 258,500 metric tonnes (*ca.* 570 million pounds), are produced in the US. This chemical finds sole use as a chemical intermediate. It is produced and used exclusively in closed systems and transport is by bulk carrier.

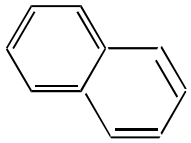
Toxics Release Inventory data reported for 1999 show that in the U.S., 118.6 metric tonnes (261,000 pounds) were released to the environment. The vast majority of this material, 118.0 metric tonnes (260,000 pounds), was released to the air, whereas 0.55 metric tonnes (1,200 pounds) were released into water. In addition to direct releases, 297.7 metric tonnes (656,000 pounds) were transferred to publicly owned treatment facilities and another 328.9 metric tonnes (725,000 pounds) to other off-site locations giving a total off-site waste transfer of approximately 626.6 metric tonnes (1,382,000 pounds).

In view of its primary use as a chemical intermediate, its low persistence in the environment, its low potential for adverse environmental impacts, and the unlikely occurrence of human exposure except in occupation situations, isobutanal is considered to be of low priority for further work.

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Isobutanal is currently of low priority for further work for human health and the environment.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	91-20-3
Chemical Name	Naphthalene
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

The chemical is a candidate for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Western European production capacity for naphthalene in 1985 was 282,000 tonnes. Around 70% is used in the manufacture of phthalic anhydride. It is also used in the production of mothballs, azo dyes, naphthalene sulfonic acids and alkylated naphthalene solvents. Naphthalene and its alkyl homologues are the major constituents of creosote used for timber treatment. Tar containing naphthalene is also used in some specialist paints and waterproof membranes. Environmental releases of naphthalene from production and use are likely to be small in comparison to releases from combustion sources, particularly motor vehicle exhausts.

In the atmosphere, naphthalene reacts with hydroxyl radicals and has a half-life of approximately 1 day. Experimental results on biodegradability indicate that naphthalene may be easily degraded under aerobic and denitrifying conditions, particularly when acclimated microorganisms are present, with concentrations falling below measurable levels in 8-12 days. Measured soil organic carbon-water partition coefficients indicate moderate sorption to soils. Bioconcentration factors of ~300 have been measured in fish.

The toxicity of naphthalene has been tested on a wide range of fish and aquatic invertebrate species. The majority of results from short-term tests lie in the range 1-10 mg/l. From longer-term studies, NOECs of 0.12 and 0.45 mg/l for fish, and 0.6 and 0.22 mg/l for invertebrates have been determined. (There are some indications from other less clear tests of effects down to 10 µg/l.) Test results for algae appear to show short-term effects at lower concentrations than those from longer-term tests. Thus growth was affected at 400 µg/l over 3 days, but 10 day EC_{50} values for biomass were 33 and 25 mg/l.

Following a detailed risk assessment in the European Union, this chemical is currently considered of low priority for further work for the environment (but see note under summary of further work).

There is no information on the effects of naphthalene following acute inhalation or dermal exposure in humans. Acute oral exposure to naphthalene causes haemolytic anaemia, which may be fatal. There is little quantitative human acute toxicity information available, although severe haemolytic anaemia, which may have proved lethal in the absence of clinical intervention, was reported in a female who had ingested approximately 6 g naphthalene (estimated to be equivalent to approximately 120 mg/kg, assuming a 50 kg youth). Studies in rodents have indicated that the toxic effects of naphthalene seen in these species are different from those in humans. No conclusions can be drawn regarding the irritant properties of naphthalene from studies in humans; data from animal studies indicate that it is only a slight skin and eye irritant. Despite widespread use, the absence of reports in humans appears to indicate

that naphthalene in not a skin or respiratory sensitiser. In animal skin sensitisation studies, negative results were obtained in both an inadequate maximisation study and a briefly reported Buehler study.

For repeated exposures via the oral route general signs of toxicity and death were observed in rats and rabbits at doses of 700 mg/kg/day and above. A NOAEL of 53 mg/kg/day was identified in mice (14 and 90 days). Signs of nasal inflammation were observed in a 90-day inhalation study in rats at 58 ppm. In mice signs of respiratory tract inflammation were noted at 10 ppm (LOAEL). No adverse effects were observed in rats following dermal application at a dose of 1000 mg/kg/day.

Naphthalene has given reproducible negative results in bacterial mutation assays, and was apparently negative in an *in vitro* UDS assay available in abstract form only. It was found to be clastogenic in CHO cells in the presence, but not in the absence, of S9; and sister chromatic exchanges were produced *in vitro* in the presence and absence of S9. This activity is not expressed *in vivo* as evidenced by the two negative micronucleus tests. However, a confirmatory *in vivo* study in a second tissue is recommended to remove uncertainty as to whether or not naphthalene has the potential to exhibit its genotoxic potential *in vivo*.

In the most useful animal carcinogenicity study available, female mice showed an increase in the incidence of benign tumours (alveolar/bronchiolar adenomas), to which this species is prone, following inhalation exposure to naphthalene. Although some uncertainty remains concerning the genotoxic potential *in vivo* of naphthalene, the neoplasia seen in mice lies on a background of inflammatory changes in the tissues affected and is thus considered to be a result of chronic tissue injury, and therefore arising via a non-genotoxic mechanism.

No animal studies have specifically investigated fertility. However, in a two-year carcinogenicity study mice showed no histopathological changes in the gonads or accessory sex organs following inhalation of 30 ppm naphthalene. Naphthalene only produces fetotoxicity at maternally toxic doses in animals, and does not produce developmental toxicity at maternally subtoxic doses.

A detailed risk assessment in the European Union has identified occupational health risks from mothball manufacture. Exposure of infants to textiles (clothing/bedding) that have been stored for long periods with naphthalene moth repellent also raises significant concern. There is documented evidence for the development of severe haemolytic anaemia resulting from such use, although there is no quantitative information available on the level or duration of exposure to naphthalene in these cases.

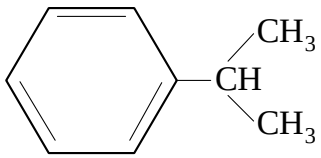
NATURE OF FURTHER WORK RECOMMENDED

SIAM 5 recommendations:

- Surveillance programme has been proposed for workers in the production of mothballs.
- Actual exposure data during damp-proof laying.
- An additional *in vivo* genotoxicity test is recommended as post-SIDS testing.
- Risk management measures should be considered concerning the exposure of infants to textiles that have been stored for long periods with naphthalene moth repellent.

[Supplementary information post-SIAM: It is recommended that Member States consider a national environmental risk assessment for use in grinding wheel manufacture.]

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	98-82-8
Chemical Name	Cumene
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

This risk assessment only covers the life cycle of cumene production and use. The potential risks related to the natural occurrence of cumene in petroleum products have not been assessed.

Environment: There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Human Health: There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Environment

Cumene is used in chemical industry in categories 2 (basic chemicals) and 3 (chemical used in synthesis). The compound is mainly used as an intermediate in the production of phenol and acetone. It is also a minor constituent of gasoline and solvents, but its presence should not be regarded as an additive but as an integrated ingredient from a petroleum derivative. The risks related to the presence of cumene in petroleum products cannot be evaluated independently for cumene but considering the presence of several other non-polar narcotic hydrocarbons in the mixture, therefore these risks have not been included in this assessment.

Cumene is a volatile compound, practically insoluble in water, inherently biodegradable and bioaccumulative. PEC values were estimated using the data provided by the industry and default values when required. The highest PEC local values for water, sediment and soil are 7.13 µg/l; 143 µg/kg; and 181µg/kg respectively. Following the previous recommendation, two new studies on the chronic toxicity of cumene on daphnia and algae respectively were presented. The chronic NOEC for fish was estimated by the sponsor country using QSARs. The recalculated PNEC values are 22 µg/l; 388 µg/kg; and 340 µg/kg for aquatic, sediment dwelling and soil dwelling organisms respectively. Therefore, it is concluded that the environmental risks associated to the life cycle of cumene production and use is low.

Human Health

Acute exposure to high concentrations of cumene can produce respiratory irritation and CNS depression. A NOAEL of 100 ppm is obtained from a subchronic toxicity study involving exposure to cumene vapour. In this study, the

observed effects at a dose above the NOAEL (500 ppm) are weak and a mild toxicity response it is obtained at a dose 10 times the NOAEL (1200 ppm). This study has been carried out in rats proved being one of the most sensitive animal species to cumene. Cumene's toxicokinetics does not seems qualitative different between human and animals. No evidence for the accumulation following repeated dose was observed. Due to these reasons, this NOAEL is considered reliable.

Comparing the worst case estimated occupational exposure level with the NOAEL it is concluded that the potential risk for workers is low.

Current information indicates that there is no use of cumene in any consumer's product. Therefore, cumene is not of concern for consumers.

Consumer's exposure to cumene respecting its use as constituent of gasoline and solvents should be assessed when a petroleum products risk assessment report will be elaborated.

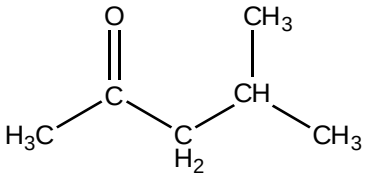
With respect to man exposed via the environment, most of the environmental exposure to cumene is predicted to be from the air contributing some 97% of the total intake. Comparing the local atmospheric concentrations of cumene identified as reasonable worst case level with the observed NOAEL it is concluded that the potential risk is low

The substance is of low concern for human health.

NATURE OF FURTHER WORK RECOMMENDED

No further work is recommended.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	108-10-1
Chemical Name	Methyl Isobutyl Ketone
Structural Formula	

CONCLUSIONS AND RECOMMENDATIONS

It is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

Methyl Isobutyl Ketone (MIBK) estimated annual production was of the order of 60,000-80,000 metric tonnes in the US, and 290,000-310,000 metric tonnes in 1995-96, worldwide. The major use of MIBK is as an industrial or commercial solvent used in paints and coatings formulations. It is also used as a chemical intermediate and as a process solvent. MIBK is typically manufactured via an enclosed, continuous process, via the aldol condensation of acetone, to form diacetone alcohol. Diacetone alcohol is subsequently dehydrated to a site-limited intermediate, mesityl oxide which is subsequently hydrogenated to MIBK. For internal plant uses, MIBK is transported through closed pipelines and stored in tanks. MIBK is transported by bulk tank cars and trucks.

MIBK is not expected to persist in the environment. In water, MIBK has been shown to be readily biodegradable. MIBK is expected to volatilize rapidly from water or soil, where rapid photodegradation would occur. Bioconcentration is not expected to be an important fate process. MIBK has a low degree of toxicity for aquatic organisms. The lowest reported toxicity threshold for any species is 136 mg/l (8day IC50(blue algae)). Toxicity to higher order plants has not been reported.

MIBK has been studied extensively, showing a low degree of toxicity by oral, dermal or inhalation routes. MIBK has been shown to be a slight dermal irritant and can be expected to be no more than moderately irritating to eyes. In several studies with human volunteers exposed to up to 200 ppm, MIBK caused reversible irritation and CNS symptoms.

The major effects noted from repeated exposures to high concentrations of MIBK were associated with the liver and kidney. In a 13-week oral study in rats, the NOAEL was determined to be 250 mg/kg, and in a 14-week inhalation study in mice and rats, the NOAEL was 1000 ppm.

In inhalation developmental toxicity studies in rats and mice, maternal toxicity and fetotoxicity were seen at 3000 ppm. Effects in the dams included decreased body weight gain, increased liver and kidney weights, decreased food consumption, and in mice, maternal deaths. Reduced fetal body weights and delayed ossification were noted in both species. Increased resorptions were noted for mice. 1000 ppm was considered to be the NOEL for both maternal animals and offspring. In an additional study, exposures of rats and mice for up to 1000 ppm 6hr/d, 5days/week for 14 weeks did not affect testicular

weights or histology of male or female reproductive organs.

Available data on MIBK indicate that it may result in some neurological effects and may enhance the neurotoxicity of other chemicals. Most genotoxicity studies show negative results for MIBK. For example, MIBK was negative in a Salmonella reverse mutation test, a cell transformation assay using BALB/3T3 cells, an unscheduled DNA synthesis assay, and a mouse bone marrow micronucleus test.