FOREWORD INTRODUCTION

Benzene, 1-chloro-2-(chloromethyl)-

CAS N°: 611-19-8

SIDS Initial Assessment Report

For

SIAM 17

Arona, Italy, 11-14th November 2003

1. Chemical Name:	Benzene, 1-chloro-2-(chloromethyl)-
2. CAS Number:	611-19-8
3. Sponsor Country:	Japan Contact Point: Mr. Yasuhisa Kawamura Director Second International Organizations Division Ministry of Foreign Affairs, Japan 2-2-1 Kasumigaseki, Chiyoda-ku, Tokyo 100-8919
4. Shared Partnership with:	Ihara Chemical Industry Co., Ltd. (sponsor) Clariant GmbH (consortia) Tessenderlo Chemie N.V (consortia)
5. Roles/Responsibilities of the Partners:	
• Name of industry sponsor /consortium	Ihara Chemical Industry Co., Ltd. 4-26, Ikenohata, 1-Chome, Taito-ku, Tokyo, Japan Phone: +81 3 3822 5253, Telefax: +81 3 3822 2497 Clariant GmbH Stroofstraße 27, 65933 Frankfurt am Main, Germany Phone: +49 (0) 69 3800 2721, Telefax: +49 (0) 69 3800 2707 Tessenderlo Chemie N.V. Rue du Trône n° 130, B-1050 Brussels, Belgium Phone: +32 2 639 18 11, Telefax: +32 2 639 19 99
• Process used	The industry consortium collected new data, prepared the updated IUCLID and drafted versions of the SIAR and SIAP.
6. Sponsorship History	
• How was the chemical or category brought into the OECD HPV Chemicals Programme ?	This substance is sponsored by Japan under the ICCA Initiative and is submitted for first discussion at SIAM 17.
7. Review Process Prior to the SIAM:	Japanese government peer-reviewed the documents, audited selected studies.

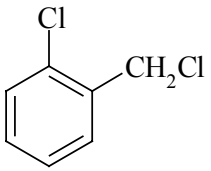
8. Quality check process: Japanese government peer-review committee performed spot checks on randomly selected endpoints and compared original studies with data in the SIDS dossier.

9. Date of Submission: 30 January 2004

10. Date of last Update:

11. Comments: The SIDS Initial Assessment Documents were prepared by Chemicals Evaluation and Research Institute (CERI), Japan.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	611-19-8
Chemical Name	Benzene, 1-chloro-2-(chloromethyl)-
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

No data are available regarding toxicokinetics, metabolism and distribution of 1-chloro-2-(chloromethyl)benzene (*o*-chlorobenzyl chloride; OCBC).
The acute inhalation LC_{50} value in male/female rats was 2.8 mg/l [OECD TG 403]. The acute dermal LD_{50} values were 1,700 (male) and 2,200 mg/kg bw (female) in rabbits and higher than 2,000 mg/kg bw in rats of both sexes. The oral LD_{50} values in rats were in the range of 350 and 951 mg/kg bw. OCBC primarily caused irritation-related histological damage to a tissue where the substance was administered; lung by inhalation, skin by dermal application and stomach by oral administration.
OCBC is irritating but not corrosive to the skin of rabbits [OECD TG 404]. The substance is also irritating to the eyes of rabbits [OECD TG 405]. Respiratory irritation was noted for OCBC with the RD_{50} value of 32.9 mg/m^3 for male mice. There are no reliable data available for sensitisation of OCBC.

In an inhalation repeated dose toxicity study [OECD TG 412], rats were exposed to OCBC vapour for 6 hours a day for 4 weeks (5 days/week) at concentrations of 0, 0.01, 0.03 and 0.10 mg/l. At 0.10 mg/l, signs indicative of irritation to the respiratory tract such as enlarged tracheobronchial lymph nodes, increased lung weights, damage to the nasal mucosa, tracheas and bronchi, and lymphoid hyperplasia in the tracheobronchial lymph nodes were observed. There was no treatment-related change in rats exposed at 0.01 and 0.03 mg/l. The NOAEL for inhalation repeated dose toxicity was determined to be 0.03 mg/l in rats of both sexes.
In an oral repeated dose toxicity study performed as a combined repeat dose and reproductive/developmental toxicity screening test [OECD TG 422], OCBC was administered by gavage to rats at doses of 0, 2, 10 and 50 mg/kg bw/day. The administration periods were 45 days for males and 41-48 days for females including all the periods between pre-mating and post-delivery. Thickening of the forestomach wall, and squamous epithelium hyperplasia, erosion and ulceration in the forestomach were observed in males at 10 and 50 mg/kg bw/day and in females at 50 mg/kg bw/day. Histological changes in the kidney, such as increases in the numbers of hyaline droplets in the proximal tubular epithelium, eosinophilic bodies, granular casts and basophilic tubules, were also observed in males at 50 mg/kg bw/day. The NOAEL for oral repeated dose toxicity was considered to be 2 mg/kg bw/day in male rats and 10 mg/kg bw/day in female rats.

One bacterial mutation study revealed that OCBC was negative with or without exogenous metabolic activation. Another bacterial mutation study showed weakly positive response without metabolic activation but negative with metabolic activation [OECD TG 471]. An *in vitro* chromosome aberration test using CHL/IU cells was positive in the presence or absence of an exogenous metabolic activation system only at cytotoxic concentrations [OECD TG 473]. The micronucleus assay using male and female rats was negative tested up to the maximum tolerated dose [OECD TG 474]. Based on the weight of evidence, OCBC is not anticipated to be genotoxic *in vivo*.

There is no data available for carcinogenicity of OCBC.

As for reproductive/developmental toxicity, no effect of OCBC was observed on any reproductive and developmental parameters in the above-mentioned combined repeat dose toxicity study at doses up to 50 mg/kg bw/day [OECD TG 422]. Thus the NOAEL for reproductive/developmental toxicity was considered to be 50 mg/kg bw/day in rats.

Environment

OCBC has a water solubility of 100 mg/l at 25°C, a vapour pressure of 0.2 hPa at 25°C and a Log K_{OW} of 3.32. The K_{OC} of 856 indicates a moderate potential of the substance for adsorption to soil and sediment. The half life of OCBC by reaction with OH radicals in air was calculated to be 103 hr. A bioconcentration factor of 71.85 was calculated for OCBC, indicating that the bioaccumulation potential of the substance is low. In the biodegradation test [OECD TG 301C], OCBC is not readily biodegradable (BOD 0% after 28 days). OCBC is hydrolyzed in water via an abiotic process to generate *o*-chlorobenzyl alcohol, which is then slowly biotransformed by oxidation to *o*-chlorobenzoic acid via *o*-chlorobenzaldehyde. An inherent biodegradability test [OECD TG 302B] showed that OCBC is inherently biodegradable with adapted industrial sludge.
The distribution of OCBC released into a particular environmental compartment was estimated with a fugacity-based model, Mackay level III. The model predicted that OCBC released into water is distributed to water (73.5 %), air (12.2%), sediment (7.7%) and soil (6.6%) while the substance released into air is distributed mainly to air (64.1%) and soil (34.6%). Almost all of the substance (99.8%) released into soil, on the other hand, was predicted to remain in its original compartment.

Acute toxicity studies with algae, invertebrates and fish have been reported. The results obtained from these studies are the 72-hr EC_{50} of 0.78 mg/l (biomass) and 1.2 mg/l (growth rate) for *Selenastrum capricornutum* [OECD TG 201], the 48-hr EC_{50} of 0.38 mg/l for *Daphnia magna* [OECD TG 202], and the 96-hr LC_{50} of 0.27 mg/l for *Oryzias latipes* [OECD TG 203].
A chronic toxicity test was performed with *Daphnia magna* [OECD TG 211]. The 21-day NOEC for its reproduction was 0.020 mg/l. The 72-hr NOEC for the growth of *Selenastrum capricornutum* based on the biomass and growth rate were 0.045 and 0.18 mg/l, respectively [OECD TG 201]. No chronic toxicity results with fish are available.
Based on the stability of OCBC in water (half-life, 33.1 hours at pH7), considerable hydrolysis of OCBC to *o*-chlorobenzyl alcohol is anticipated. Thus the aquatic effect of *o*-chlorobenzyl alcohol was taken into consideration. Although no toxicity data is available for this substance, the analysis by ECOSAR (ECOWIN v0.99g) showed 96-hr LC_{50} of 15.7-189.7 mg/l for fish and 48-hr LC_{50} of 0.3-0.6 mg/l for Daphnia, suggesting that *o*-chlorobenzyl alcohol is not more toxic to aquatic organisms than OCBC. Consistent with this prediction, the 96 hr LC_{50} values (nominal) of OCBC for fish obtained in a static system (0.5-0.71 mg/l for *Danio rerio* and 0.71-0.96 mg/l for *Pimephales promelas*) were higher than that obtained in a flow-through system (0.27 mg/l for *Oryzias latipes*).

Exposure

In 2002 the chemical was produced in Germany, Japan and Belgium. The total production volume was about 1,000 tonnes per year for the last five years. In each country, only one company, which has one production site, currently operates the production of the substance.
OCBC is produced by chlorination of *o*-chlorotoluene in a closed system. There is no process that generates waste water in the production of OCBC. The waste residue is incinerated. The off-gas of the reaction is incinerated or treated on active carbon. Therefore there is no release of OCBC to the environment from its manufacturing plants.
The use pattern of OCBC is also limited to the use as an intermediate for the production of agrochemicals. In the Sponsor country, only one agrochemical is manufactured from OCBC in a closed system. Because OCBC is reacted away in the process, there is no release of OCBC from the production site of the agrochemical. No contamination of OCBC is detected in the agrochemical (detection limit 0.002%). OCBC is not detected in soil as degradation products of agrochemicals. Based on these facts, it is considered that the impact of OCBC to the environment (aquatic and terrestrial) is negligible.
In Japan, the number of workers engaged in manufacturing and processing of the substance at the production site is limited to less than twenty, and the operation period at the plant is also limited (approx. 2-6 weeks/year in 1999-2003). The monitoring data revealed that the OCBC concentrations in the air of workplace atmospheres at the production site were minimal. Furthermore, workers are obliged to use personal protection equipments such as mask, safety glasses and gloves during the operation. At the user site in the sponsor country, the number of workers and the operation period is also limited, and OCBC is treated in a similar way than at the production sites. Therefore, occupational exposure to OCBC is considered to be minimal.
Consumer exposure is also considered negligible because no contamination of OCBC is detected in the product manufactured from OCBC in the sponsor country.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

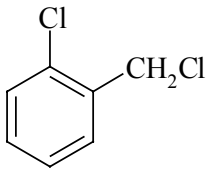
The chemical possesses properties indicating a hazard for human health (repeated dose toxicity) and the environment. Based on data presented by the Sponsor country, exposure to humans and the environment is anticipated to be low, and therefore this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 611-19-8
IUPAC Name: 1-Chloro-2-(chloromethyl)benzene
Molecular Formula: $C_7H_6Cl_2$
Structural Formula:



Molecular Weight: 161.03
Synonyms: *o*-Chlorobenzyl chloride (OCBC)

Benzene, 1-chloro-2-(chloromethyl)-

alpha, 2-Dichlorotoluene

alpha, *o*-Dichlorotoluene

1-Chloro-2-(chloromethyl)benzene

2-Chlorobenzyl chloride

o, alpha-Dichlorotoluene

Toluene, *o*, alpha-dichloro-

alpha, 2-Dichlortoluol

alpha-2-diclorotolueno

1.2 Purity/Impurities/Additives

Purity

> 99 %

Impurities

2-Chlorobenzaldehyde	0.01 %
alpha, 4-Dichlorotoluene	0.2 %
1-Chloro-2-(dichloromethyl)benzene	0.06 %

1.3 Physico-Chemical properties

Table 1 Summary of physico-chemical properties

Property	Value	Protocols (Reference) or comments
Physical state	Liquid	
Melting point	-17°C	Unknown (CRC Handbook 2nd ed.)
Boiling point	217°C (1013 hPa)	Unknown (CRC Handbook 2nd ed.)
Relative density	1.274	Density: 1.2743 g/cm^3 at 20°C (Hammond, 1949)
Vapour pressure	0.2 hPa (25°C)	Calculated (MPVPWIN V1.40, 2003)
Water solubility	100 mg/l (25°C)	OECD TG 105 (CERI, 1999a)
Partition coefficient n-octanol/water (log value)	3.32	OECD TG 107 (CERI, 1999b)
Henry's law constant	157 Pa m^3/mol (25°C)	Calculated (HENRYWIN ver.3.10, 2003)

1-Chloro-2-(chloromethyl)benzene (*o*-Chlorobenzyl chloride; OCBC) is a clear and colorless liquid with a pungent odor.

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

Production Volumes

The annual production of *o*-chlorobenzyl chloride (OCBC) in Germany, Japan and Belgium is summarized in Table 2-1 (Ihara Chem. Ind., 2003; Clariant GmbH, 2003a, Tessenderlo Chemie N. V., 2003). In these countries, only one company, which has one production site, currently operates the production of OCBC. The total production volume was about 1,000 tonnes per year for the last five years. Although the chemical may be produced in China, no data is available for the country's production quantity.

Table 2-1 Annual production of OCBC.

Year	Production volume (tonnes)		
	Germany	Japan	Belgium
1999	140	156	0
2000	700	390	0
2001	350	431	653
2002	180	330	552
2003	No data available	149	No data available

OCBC is produced by chlorination of *o*-chlorotoluene in a closed system (Ihara Chem. Ind., 2003; Clariant GmbH, 2003a; Tessenderlo Chemie N. V., 2003).

Use Pattern

OCBC is used only as an intermediate for the production of agrochemicals (Ihara Chem. Ind., 2003; Clariant GmbH, 2003a; Tessenderlo Chemie N. V., 2003). The agrochemicals manufactured from

OCBC are only two herbicides in OECD countries. The total amount of OCBC produced is used for the production of these herbicides.

2.2 Environmental Exposure and Fate

2.2.1 Sources of Environmental Exposure

There is no process that generates waste water in the production of OCBC. The waste residue is incinerated. The off-gas of the reaction is incinerated or treated with active carbon. Therefore there is no release of OCBC to the environment from its manufacturing plants (Ihara Chem. Ind., 2003; Clariant GmbH, 2003a; Tessenderlo Chemie N.V., 2003).

In the sponsor country, there is only one user site, which is located near the production site. At this site, only one agrochemical is manufactured from OCBC in a closed system. As OCBC is reacted away in the process, there is no release of OCBC to the environment from the production site of the agrochemical (Ihara Chem. Ind., 2003).

The use of agrochemicals manufactured from OCBC might be the source of environmental exposure of OCBC. This exposure scenario is not expected in the sponsor country, however, because no contamination of OCBC is detected in the final product (detection limit 0.002%) and OCBC is not detected as a degradation product of agrochemicals in soil (Ihara Chem. Ind., 2003; Ikeda et al., 1986; FMC, 2003).

2.2.2 Photodegradation

The half-life of OCBC by reaction with OH radicals in air was calculated to be 103 hr (assuming a 12hr day and an OH concentration of 1.5 x 10^6 molecule/cm^3). The reaction rate constant was estimated to be 1.2454 x 10^{-12} cm^3/molecule/sec (AOPWIN ver.1.90, 2003).

2.2.3 Stability in Water

The stability of OCBC in water was examined according to OECD TG 111. OCBC was hydrolyzed to *o*-chlorobenzyl alcohol at 25°C with half-lives of 34.9, 33.1 and 36.4 hours at pH 4.0, 7.0 and 9.0, respectively (CERI, 1999a, 1998).

2.2.4 Transport between Environmental Compartments

Taking the following physico-chemical properties of OCBC into consideration, it is suggested that OCBC released into the environment is distributed into all the environmental compartments; air, water, soil and sediment. The physico-chemical property values used for the modelling are: water solubility = 100 mg/l (measured; CERI, 1999a), vapour pressure = 0.2 hPa (calculated; CERI, 2003), Partition Coefficient ($LogP_{OW}$) = 3.32 (measured; CERI, 1999b), Henry's law constant = 157 Pa m^3/mol (calculated; CERI, 2003) and soil adsorption coefficient (K_{OC}) = 856 (calculated; CERI, 2003). This adsorption coefficient indicates a moderate potential of the substance for adsorption to soil and sediment.

The distribution of OCBC released into a particular compartment was estimated with a fugacity-based model, Mackay level III (CERI, 2003). The half-life in the different compartments used in the modelling are 103 hr (estimated), 33 hr (measured), 240,000 hr (default) and 720,000 hr (default) in air, water, soil and sediment, respectively. The results are shown in Table 2-2. The model predicted that OCBC released into water is distributed into water (73.5 %), air (12.2%), sediment (7.7%) and soil (6.6%) while OCBC released into air is distributed mainly into air (64.1%) and soil (34.6%).

Almost all of the substance (99.8%) released into soil, on the other hand, was predicted to remain in its original compartment.

Table 2-2. Estimation of environmental distribution of OCBC with a generic Fugacity model, Mackay level III.

Compartment	Release		
	100% to air	100% to water	100% to soil
Air	64.1%	12.2%	0.2%
Water	1.1%	73.5%	0.0%
Soil	34.6%	6.6%	99.8%
Sediment	0.1%	7.7%	0.0%

2.2.5 Biodegradation

The biodegradation of OCBC by an activated sludge in 28 days was tested according to OECD TG 301C. The determination by the BOD and TOC methods showed 0% degradation of OCBC. The analysis by HPLC, however, indicated that all the substance was transformed, generating *o*-chlorobenzyl alcohol (92%), *o*-chlorobenzaldehyde (2%) and *o*-chlorobenzoic acid (3%) (CERI, 1998). The test without the activated sludge also indicated that OCBC was completely converted to *o*-chlorobenzyl alcohol without further transformation. Based on these observations, it is concluded that OCBC is hydrolyzed in water via an abiotic process to generate *o*-chlorobenzyl alcohol, which is then slowly biotransformed by oxidation to *o*-chlorobenzoic acid via *o*-chlorobenzaldehyde. Therefore OCBC and its hydrolysis products are not readily biodegradable.

An inherent biodegradability test was conducted according to OECD TG 302B (Wellens H., 1990). A mixture containing OCBC, mineral nutrients and an industrial activated sludge was agitated with aeration. This test was adapted to the volatility of a test substance by using a respirometric method to determine the biodegradation instead of DOC measurement. Thus the result was not influenced by volatilisation if any. The test showed 99% degradation of OCBC after 9 days. The adaptation period lasted 6 days (less than 10% degradation) and 90% degradation of OCBC was observed in the last 3 days. Thus, OCBC is inherently biodegradable with adapted industrial sludge.

2.2.6 Bioaccumulation

The bioconcentration factor for OCBC was calculated to be 71.85 (BCFWIN v 2.14) with a measured log K_{OW} of 3.32, indicating that accumulation of the substance in aquatic organisms is unlikely.

2.2.7 Other Information on Environmental Fate

No other information on environmental fate is available.

2.3 Human Exposure

2.3.1 Occupational Exposure

There is no Occupational Exposure Limit (OEL) for OCBC in Japan, Germany and Belgium. In each country, only one company, which has one production site, currently produces OCBC. The

number of workers engaged in manufacturing and processing of OCBC is limited to less than twenty in each country (Ihara Chem. Ind., 2003; Clariant GmbH, 2003a; Tessenderlo Chemie N.V., 2003). Furthermore, in Japan and Germany, the number of operation days at the site is also limited (Japan; approx. 2-6weeks/year in 1999-2003, Germany; approx. 3-24 weeks/year) (Ihara Chem. Ind., 2003; Clariant GmbH, 2003a). The production of OCBC is carried out in a closed system. However, there are some possibilities that the workers are exposed to OCBC via the dermal or inhalation route in the processes such as putting stabilizer and raw material into a reaction tank, sampling and preparation for GC-FID analysis, filling a drum with OCBC produced, and handling residuals/wastes from the plant.

Occupational exposure monitoring was conducted at the production site in Japan. The results are summarized in Table 2-3 (Ihara Chem. Ind., 2003). These monitoring data revealed that the OCBC concentrations in the air of various workplace atmospheres ranged from 0.008 ppm to 0.017 ppm. Practically, the production of OCBC is operated in a closed system and workers are obliged to use personal protection equipments such as mask, safety glasses and gloves during operation. Thus, the actual levels of exposure to the chemical via the dermal or inhalation routes are expected to be minimal.

At the user site in the sponsor country, OCBC is used as the intermediate for the production of an agrochemical in a closed system and treated in a way similar to that at the production site. Putting OCBC into a reaction tank is the only process that might cause occupational exposure at the user site because OCBC is reacted away in the production of the agrochemical and no contamination of OCBC is detected in the final product (detection limit 0.002%). This process is just like a reverse process of filling drums with OCBC at the production site. Thus the OCBC concentrations in the air of workplace atmospheres at the user site are anticipated to be at the same level or less than at the production site. Furthermore, workers at the user site are also obliged to use personal protection equipments such as mask, safety glasses and gloves during operation. Based on these facts, the occupational exposure situation at the user site is comparable to the situation at the production site in the sponsor country. Therefore the occupational exposure to OCBC is also considered to be negligible in the sponsor country (Ihara Chem. Ind., 2003).

Table 2-3. Concentration of OCBC in the air of workplace atmosphere

Work Process	Working time	Mean Conc. (ppm)
Putting stabilizer in a tank	10 sec./3days	ND (<0.013)
Putting raw material in a tank	10 sec./day	ND (<0.017)
Sampling and preparation for GC-FID analysis	20 min./day	0.0153
Filling a drum	6.5 hrs./day 3 min./drum	0.008
Treatment of waste oil (residual)	5 min./day	ND (<0.013)

ND: not detected

2.3.2 Consumer Exposure

The use of OCBC is limited to intermediates for producing agrochemicals. The agrochemicals manufactured from OCBC are only two herbicides in OECD countries. In the sponsor country, only one herbicide is produced and used. No contamination of OCBC is detected in this herbicide by GC analysis (detection limit 0.002%). Therefore, consumer exposure is considered negligible in the sponsor country (Ihara Chem. Ind., 2003Clariant GmbH, 2003a; Tessenderlo Chemie N. V., 2003).

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

There are no data available for toxicokinetics, metabolism, and distribution of *o*-chlorobenzyl chloride (OCBC).

3.1.2 Acute Toxicity

Available data for acute toxicity of OCBC are summarized in Table 3-1.

Table 3-1. Summary of acute toxicity studies.

Species, strain	Route	Type	Value	Reference
Rat, Wistar	Inhalation (aerosol)	LC_{50}	M & F: 2.8 mg/l 4hour	Clariant GmbH, 1987
Rat, Wistar	Inhalation (vapour)	LC_{50}	M & F: > 1.14 mg/l 60min	Occidental Chem. Corp., 1990a
Rat, SD	Dermal	LD_{50}	M & F: > 2,000 mg/kg bw	Ihara Chem. Ind., 1993b
Rabbit, N.Z.White	Dermal	LD_{50}	M: 1,700 mg/kg bw F: 2,200 mg/kg bw	Monsanto Co., 1992
Rat, SD	Oral	LD_{50}	M: 951 mg/kg bw F: 783 mg/kg bw	MHLW Japan, 1999a
Rat, SD	Oral	LD_{50}	M: 690 mg/kg bw F: 533 mg/kg bw	Ihara Chem. Ind., 1993a
Rat, SD	Oral	LD_{50}	M: 880 mg/kg bw F: 350 mg/kg bw	Monsanto Co., 1992
Rat, SD	Oral	LD_{50}	M & F: 430 mg/kg bw	Occidental Chem. Corp., 1990a

Studies in Animals

Inhalation

There are two reliable studies on acute inhalation toxicity.

A study on acute inhalation toxicity in rats was carried out under OECD TG 403 in compliance with GLP (Clariant GmbH, 1987). Rats (5 animals/sex/group) were exposed (mouth/nose only) continuously for 4 hours to OCBC aerosol at concentrations of 0.587, 1.548, 1.648, 2.716, 5.268 and 5.723 mg/l, and observed for 14 days. Death occurred at 1.548 mg/l and higher. The LC_{50} value was estimated to be 2.8 mg/l in both sexes. Clinical signs observed were gasping respiration, respiratory sounds, uncoordinated, ataxic and stilted gait, cyanosis, stupor, squatting posture, prone position, flanks pinched in, nose and lid margin red-encrusted, corneal opacity, and narrow palpebra fissure.

The other study on acute inhalation toxicity in rats was conducted by a method basically equivalent to OECD TG 403 in compliance with GLP (Occidental Chem. Corp., 1990a). Rats (10 animals/sex/group) were exposed systemically for 1 hour to OCBC vapour at a concentration of

1.140 mg/l and observed for 14 days. No animal death occurred during the observation period, indicating that the LC_{50} value is over 1.140 mg/l. Clinical signs as described above were also observed in the OCBC-treated animals. All the rats recovered to normal in 5 days after the exposure. There was no macroscopic and histopathological change observed in the animals.

Dermal

There are two reliable studies on acute dermal toxicity. Both studies were conducted according to national guideline in compliance with GLP.

In a study, OCBC was applied to shaven skin of rats (5 animals/sex) at a dose of 2,000 mg/kg bw by semi-occlusive dressing for 24 hours and the animals were observed for 14 days (Ihara Chem. Ind., 1993b). No death occurred during the observation period, indicating that the LD_{50} value is over 2,000 mg/kg bw in both sexes. Clinical signs observed were clear ocular discharge, reddened extremities, urogenital staining, soft stool and hypoactivity. The signs disappeared by day 3 or earlier. The substance also induced irritation to skin, consisting of erythema, edema, desquamation, eschar and exfoliation.

In the other study, OCBC was applied to clipped skin of rabbits (15 animals/sex/group) at doses of 1,000, 2,000, and 4,000 mg/kg bw by occlusive dressing and the animals were observed for 14 days (Monsanto Co., 1992). The LD_{50} values were estimated to be 1,700 and 2,200 mg/kg bw in male and female rabbits, respectively. Clinical signs observed were reduction of food consumption, ataxia, tremors, hypopnea, hypothermia, nasal discharge, unthrify coats and urinary/fecal staining. In addition, severe dermal lesion at the application site was also noted.

Oral

There are four reliable studies on acute oral toxicity in rats. LD_{50} values in these studies were determined on the basis of 14-day observation.

A study was conducted according to OECD TG 401 in compliance with GLP (MHLW Japan, 1999a). OCBC diluted in 0.1% Tween 80 was administered by gavage to rats (5 animals/sex/group) at doses of 350, 500, 700, 1,000 and 1,400 mg/kg bw. Animal death occurred at the doses of 500 mg/kg bw and higher. The LD_{50} values were estimated to be 951 and 783 mg/kg bw in male and female rats, respectively. Clinical signs observed were salivation, lacrimation, flushing, decrease in locomotor activity, loose stool and abnormal gait. Autopsy and histopathological examination of dead animals showed erosion/ulceration of the glandular stomach and submucosal edema of the forestomach. Autopsy of surviving animals revealed thickening of the forestomach wall, erosion/ulceration of forestomach and adhesion of the organs in the abdominal cavity. Histopathological examination of the surviving animals also showed ulceration, squamous epithelium hyperplasia, inflammatory cellular infiltration and granulation tissue in the forestomach, and peritonitis in the serous membrane.

The other studies in rats were conducted according to national guidelines or according to a method equivalent to OECD TG 401. The LD_{50} values determined by the studies were as follows: 690 (male) and 533 mg/kg bw (female) (Ihara Chem. Ind., 1993a); 880 (male) and 350 mg/kg bw (female) (Monsanto Co., 1992); 430 mg/kg bw (male/female) (Occidental Chem. Corp., 1990a). In these studies, clinical signs quite similar to those observed in the MHLW study were observed. Abnormalities indicative of irritation to gastrointestinal tract as described above were also noted in the OCBC-treated animals.

Conclusion

The inhalation LC_{50} value in male and female rats was 2.8 mg/l. The dermal LD_{50} values were 1,700 mg/kg bw (male) and 2,200 mg/kg bw (female) in rabbits and higher than 2,000 mg/kg bw in

rats of both sexes. The oral LD_{50} values in rats were in the range of 350 to 951 mg/kg bw. OCBC primarily caused irritation-related histological damage to a tissue where the substance was administered; lung by inhalation, skin by dermal application and stomach by oral administration.

3.1.3 Irritation

Skin Irritation

Studies in Animals

Four reliable studies were available for skin irritation of OCBC. Two studies were conducted according to OECD TG 404 (Ihara Chem. Ind., 1992; Clariant GmbH, 1985a) and the other two studies under the method equivalent to the OECD TG (Monsanto Co., 1992; Occidental Chem. Corp., 1990a). All the studies were performed in compliance with GLP.

In the study by Ihara Chem. Ind., 0.5 ml of OCBC was applied to skin of rabbits for 3 min, 60 min or 4 hours by semi-occlusive covering (Ihara Chem. Ind., 1992). Very slight to well-defined erythema was observed in all application sites. This reaction disappeared within 7 or 10 days. Very slight to slight edema was observed only in the 4-hour application sites from 24 to 48 hours after application. No necrosis was observed in any application sites. Based on these observations, OCBC was considered to have a mild dermal irritation potential on the rabbit skin.

In the other studies, OCBC was applied to skin of rabbits for 4 hours (Clariant GmbH, 1985a; Monsanto Co., 1992; Occidental Chem. Corp., 1990a) and also for 24 hours (Monsanto Co., 1992). The 4-hour application caused mild/moderate irritation to the rabbit skin with erythema and edema. No necrosis was observed, however. The 24-hour application, on the other hand, exhibited severer irritation accompanied with blanching of the skin in addition to moderate to severe edema. The primary irritation index for the 24-hour application was 3.9.

Eye Irritation

Studies in Animals

There are three reliable studies on eye irritation of OCBC.

The study by Clariant GmbH (Clariant GmbH, 1985b) was well conducted according to OECD TG 405 in compliance with GLP. OCBC (0.1 ml) was applied to eyes of three rabbits and the eyes were rinsed 24 hours later. The animals were observed for 14 days after the application. All animals exposed to this substance showed a positive response with mild/moderate irritation to conjunctivae, iris and cornea. All the symptoms observed disappeared completely within the observation period, concluding that OCBC is mildly irritating to the eyes of rabbits.

In the other studies, 0.1 ml of OCBC was applied to eyes of rabbits with or without rinsing thereafter, and the animals were then observed for 21 days (Monsanto Co., 1992; Occidental Chem. Corp., 1990a). In either case, OCBC exhibited mild to moderate ocular irritation, which was reversible during the observation period.

Respiratory Tract Irritation

Studies in Animals

There are two reliable studies on respiratory irritation of OCBC in mice.

Male and female mice were exposed continuously for 30 minutes to OCBC vapour at concentrations of 11.9, 24.2, 82.3 and 179.5 mg/m^3 (Vijayaraghavan et al., 1993). Respiratory rates were determined with body plethysmography. Inspiratory and expiratory airflow, and tidal volume

were also measured. The potency for sensory irritation defined as the airborne concentration that caused 50 % decrease in the respiratory rate (RD_{50}) was 85 and 69 mg/m^3 for male and female mice, respectively.

In the other study, male mice were exposed continuously for 10 min to OCBC vapour at least 4 doses (concentrations unknown) (Dudek et al., 1992). Sensory irritation was determined with body plethysmography. The RD_{50} value in this study was 32.9 mg/m^3.

Conclusion

OCBC is irritating but not corrosive to the skin of rabbits. OCBC is also irritating to the eyes of rabbits. Respiratory irritation was further noted for OCBC with the RD_{50} value of 32.9 mg/m^3 for male mice.

3.1.4 Sensitisation

Studies in Animals

Skin

No reliable study on skin sensitisation of OCBC has been reported while there is one study report with low reliability (Landsteiner and Jacobs, 1936). The study was conducted in guinea pigs, suggesting that eight out of thirteen animals tested gave a positive response to OCBC. However, this study was considered invalid because the criteria for positive/negative response were not defined in the report.

Respiratory Tract

There is no study available for respiratory tract sensitisation of OCBC in animals.

Conclusion

There is no reliable data available for sensitisation of OCBC although one study suggested skin sensitisation of OCBC in guinea pigs.

3.1.5 Repeated Dose Toxicity

Studies in Animals

There are two reliable studies on repeated dose toxicity in rats; one inhalation and one oral study. The studies were conducted according to OECD Test Guidelines in compliance with GLP.

Inhalation

The repeated dose inhalation toxicity study in rats was conducted according to OECD TG 412 (Occidental Chem. Corp., 1990b). Rats (5 animals/sex/group) were exposed systemically to OCBC vapour for 4 consecutive weeks (6 hr/day, 5 days/week (Monday to Friday)) at concentrations of 0.01, 0.03 and 0.10 mg/l. No death occurred in any groups. Various toxicological findings were observed in male and female rats at 0.1 mg/l. Clinical signs indicative of irritation to the respiratory tract were observed during the exposure period. These included eyes shut/half-shut, adoption of a prone/hunched posture, rubbing of the chin on the mesh floor of the exposure chamber with licking of the inside of the mouth, red ears, agitated grooming and short periods of head shaking. Rales were noted in one male rat, during the latter half of week 4. Body weight gain, food consumption and water consumption were reduced during the exposure period. Increases in packed cell volume, hemoglobin and red cell count, and a decrease in urinary volume were also observed. The ratio of

myeloid and erythroid cells was increased. Gross autopsy revealed enlarged tracheobronchial lymph nodes and elevated lung weights. Histopathological examination showed damage to the nasal mucosa, trachea and bronchi (epithelial degeneration and hyperplasia of the nasal mucosa and the bronchiolar epitherium, squamous metaplasia of the bronchiolar epitherium), which was consistent with the irritating property of the OCBC vapour. Lymphoid hyperplasia was further observed in the tracheobronchial lymph nodes of some of the rats. There was no treatment-related change in male and female rats exposed at 0.01 and 0.03 mg/l. Based on these observations, NOAEL for inhalation repeated dose toxicity was considered to be 0.03 mg/l in both sexes.

Dermal

There is no study available for repeated dose dermal toxicity of OCBC in animals.

Oral

The repeated dose oral toxicity study in rats was conducted according to OECD TG 422 (combined repeat dose and reproductive/developmental toxicity screening test) (MHLW, Japan, 1999b). Rats (12 animals/sex/group) were given OCBC by gavage at doses of 2, 10 and 50 mg/kg bw/day. Male rats were dosed from 14 days before mating to the day before scheduled sacrifice through the mating period (total 45 days). Female rats were dosed from 14 days before mating to 4 days after delivery through the mating and gestation periods (total 41-48 days). Suppression of body weight gain and a decrease in food consumption were observed in the early period of administration in male and female rats at 50 mg/kg bw/day. Increases in the relative and absolute liver weights were also observed in females at this dose. At scheduled sacrifice, thickening of the forestomach wall was observed in males at 10 mg/kg bw/day and both sexes at 50 mg/kg bw/day. Histopathological examination revealed squamous epithelium hyperplasia, erosion and ulceration in the forestomach in males at 10 mg/kg bw/day and both sexes at 50 mg/kg bw/day. The changes observed in the forestomach were considered due to the irritating property of OCBC. In addition, increases in the numbers of hyaline droplets in the proximal tubular epithelium, eosinophilic bodies, granular casts and basophilic tubules were observed in the kidneys of males at 50 mg/kg bw/day. There was no effect on hematological and clinical examinations and organ weights in male rats in the OCBC-treated groups. Based on these observations, the NOAEL for oral repeated dose toxicity was considered to be 2 mg/kg/day in male rats and 10 mg/kg/day in female rats

Conclusion

In the inhalation toxicity study, clinical signs indicative of irritation to the respiratory tract were observed. The NOAEL for inhalation repeated dose toxicity was determined to be 0.03 mg/l in rats of both sexes. In the oral toxicity study, thickening of the forestomach wall, and squamous epithelium hyperplasia, erosion and ulceration in the forestomach were observed in male rats at 10 and 50 mg/kg bw/day and in female rats at 50 mg/kg bw/day. The NOAEL for oral repeated dose toxicity was considered to be 2 mg/kg/day in male rats and 10 mg/kg/day in female rats.

3.1.6 Mutagenicity

Available mutagenicity data of OCBC are summarized in Table 3-2.

In vivo Studies

There is one reliable study available for *in vivo* mutagenicity of OCBC.

A micronucleus assay in male and female rats was conducted according to OECD TG 474 in compliance with GLP (Clariant GmbH, 2003b). A preliminary experiment showed that no death occurred at doses of 400 and 500 mg/kg bw while death (one out of three males and two out of

three females) was observed at 600 mg/kg bw. Thus OCBC was orally administered twice at an interval of 24 hours to the animals at 50, 150 and 500 mg/kg bw. In the dose group of 500 mg/kg bw, one out of ten animals died and the following clinical signs were observed 2 to 6 hours after the second treatment; diarrhea, stilted gait and cowering posture. All the animals were sacrificed 24 hours after the second treatment and subjected to the erythrocyte micronucleus test. No statistically significant increase in the micronucleated polychromatic erythrocyte frequencies was observed in any dose groups, indicating that OCBC is not clastogenic *in vivo*.

In vitro Studies

Bacterial mutation tests:

There are two reliable studies on bacterial mutation.

A study was conducted according to OECD TG 471 in compliance with GLP (MHLW, Japan, 1999c). The effect of OCBC on reverse mutation was examined in four *Salmonella typhimurium* strains, TA98, TA100, TA1535 and TA1537, and in an *Escherichia coli* strain, WP2 *uvrA*, at concentrations up to 0.5 mg/plate with or without exogenous metabolic activation system. A marginal but dose-related increase was observed in TA100 without metabolic activation. In the presence of metabolic activation system, however, TA100 did not show any positive response. The other strains showed negative response regardless of metabolic activation. Based on these results, OCBC was considered a weak mutagen in the absence of metabolic activation but the mutagenicity was diminished or negated in the presence of the activation system.

The other bacterial mutation assay was performed according to a scientifically acceptable method in compliance with GLP (Clariant GmbH, 1983) up to higher dose levels than the MHLW study. In this study, OCBC did not show any mutagenic activity in any tester strains regardless of metabolic activation.

Chromosome aberration test:

There is one reliable study on *in vitro* chromosome aberration in Chinese hamster lung (CHL/IU) cells.

The study was conducted according to OECD TG 473 in compliance with GLP (MHLW, Japan, 1999d). The CHL/IU cells were continuously treated with OCBC for 24 or 48 hours at concentrations of 0.0013, 0.0025, 0.0050, 0.010 and 0.020 mg/ml without metabolic activation. A significant increase in polyploidy (3.38%) was observed at 0.010 mg/ml for 24 hours continuous treatment, at which concentration cytotoxicity was observed. In another assay, the CHL/IU cells were shortly (6 hours) treated with OCBC in the presence or absence of an exogenous metabolic activation system at concentrations of 0.013, 0.025, 0.050, 0.10 and 0.20 mg/ml. A significant increase in structural chromosomal aberrations (frequency: 13.0%) was observed only in the top concentration culture. These clastogenic and aneugenic activities were observed only at the highest concentration, which showed cytotoxicity, and the next lower concentration of OCBC did not induce any chromosomal aberrations.

Table 3-2 Available genetic toxicity data

	Type	System of testing	Conc./Dose	Result -S9 +S9	Reference
In vitro	Ames test	*Salmonella typhimurium* TA100, TA1535, TA98, TA1537, *Escherichia coli* WP2 *uvrA*	0.0156 – 0.5 mg/plate	+/– – (TA100)	MHLW, Japan, 1999c
			0.09 – 0.24 mg/plate	+/– – (TA100)	
		Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538, *Escherichia coli* WP2 *uvrA*	0.0008 – 1.5 mg/plate	– –	Clariant GmbH, 1983
	chromosomal aberration test	Chinese hamster lung (CHL/IU) cells	0.0013 – 0.02 mg/ml	+[a)] ND (0.01)	MHLW, Japan, 1999d
			0.013 – 0.2 mg/ml	+[a)] (0.1)	
In vivo	Micronucleus assay	SD Rat	50, 150, 500[b)] mg/kg bw	– ND	Clariant GmbH, 2003b

+: positive, +/–: equivocal, –: negative, ND: no data

a): positive at the concentration showed cytotoxicity.

b): In the dose group of 500 mg/kg bw, one out of ten animals died.

Conclusion

One bacterial mutation study revealed that OCBC was negative with or without exogenous metabolic activation. Another bacterial mutation study, on the other hand, showed a weakly positive response without metabolic activation but was negative with metabolic activation. An *in vitro* chromosome aberration test using CHL/IU cells was positive in the presence or absence of an exogenous metabolic activation system only at the cytotoxic concentrations. The micronucleus assay using male and female rats was negative up to the maximum tolerated dose. Based on the weight of evidence, OCBC is not anticipated to be genotoxic *in vivo*.

3.1.7 Carcinogenicity

There are no data available for carcinogenicity of OCBC.

3.1.8 Toxicity for Reproduction

Studies in Animals

There is one reliable study on reproductive/developmental toxicity of OCBC. This study was conducted as a combined repeat dose and reproductive/developmental toxicity screening test according to OECD TG 422 in compliance with GLP (MHLW, Japan, 1999b). OCBC was administrated by gavage to rats (12 animals/sex/group) at doses of 0 (vehicle control, 0.1% Tween 80 solution), 2, 10 and 50 mg/kg bw/day. Males were dosed from 14 days before mating to the day before scheduled sacrifice through the mating period (total 45 days). Females were dosed from 14 days before mating to 4 days after delivery through the mating and gestation periods (total 41-48 days). OCBC showed no effect on the following parental reproductive parameters; mating index, fertility index, numbers of corpora lutea and implantations, implantation index, delivery index,

gestation index, gestation length, and parturition and maternal behavior. Regarding the examination of neonates, there was no effect of OCBC on the numbers of total offspring and live offspring, sex ratio, live birth index, viability index, or body weight. Also, no compound-related abnormality was found in external features, clinical signs, or autopsy findings of offspring. Based on these observations, the NOAEL for reproductive/developmental toxicity was considered to be 50 mg/kg bw/day in rats.

Conclusion

There was no effect of OCBC observed on any reproductive and developmental parameters in rats up to 50 mg/kg bw/day. Thus the NOAEL for reproductive/developmental toxicity was considered to be 50 mg/kg bw/day in rats.

3.2 Initial Assessment for Human Health

No data are available for toxicokinetics, metabolism and distribution of OCBC.

The acute inhalation LC_{50} value in male and female rats was 2.8 mg/l. The acute dermal LD_{50} values were 1,700 (male) and 2,200 mg/kg bw (female) in rabbits and higher than 2,000 mg/kg bw in rats of both sexes. The oral LD_{50} values in rats were in the range of 350 and 951 mg/kg bw. OCBC primarily caused irritation-related histological damage to a tissue where the substance was administered; lung by inhalation, skin by dermal application and stomach by oral administration.

OCBC is irritating but not corrosive to the skin of rabbits. OCBC is also irritating to the eyes of rabbits. Respiratory irritation was noted for OCBC with the RD_{50} value of 32.9 mg/m^3 for male mice. There are no reliable data available for sensitisation of OCBC.

In an inhalation repeated dose toxicity study, rats were exposed to OCBC vapour for 6 hours a day for 4 weeks (5 days/week) at concentrations of 0, 0.01, 0.03 and 0.10 mg/l. At 0.10 mg/l, signs indicative of irritation to the respiratory tract such as enlarged tracheobronchial lymph nodes, elevated lung weights, damage to the nasal mucosa, tracheas and bronchi, and lymphoid hyperplasia in the tracheobronchial lymph nodes were observed. There was no treatment-related change in rats exposed at 0.01 and 0.03 mg/l. The NOAEL for inhalation repeated dose toxicity was determined to be 0.03 mg/l in rats of both sexes.

In an oral repeated dose toxicity study performed as a combined repeat dose and reproductive/developmental toxicity screening test, OCBC was administered by gavage to rats at doses of 0, 2, 10 and 50 mg/kg bw/day. The administration periods were 45 days for males and 41-48 days for females including all the periods between pre-mating and post-delivery. Thickening of the forestomach wall, and squamous epithelium hyperplasia, erosion and ulceration in the forestomach were observed in males at 10 and 50 mg/kg bw/day and in females at 50 mg/kg bw/day. Histological changes in kidney, such as increases in the numbers of hyaline droplets in the proximal tubular epithelium, eosinophilic bodies, granular casts and basophilic tubules, were also observed in males at 50 mg/kg bw. The NOAEL for oral repeated dose toxicity was considered to be 2 mg/kg bw/day in male rats and 10 mg/kg bw in female rats.

One bacterial mutation study revealed that OCBC was negative with or without exogenous metabolic activation. Another bacterial mutation study, on the other hand, showed weakly positive response without metabolic activation but negative with metabolic activation. An *in vitro* chromosome aberration test using CHL/IU cells was positive in the presence or absence of an exogenous metabolic activation system only at the cytotoxic concentrations. The micronucleus assay using male and female rats was negative up to the maximum tolerated dose. Based on the weight of evidence, OCBC is not anticipated to be genotoxic *in vivo*.

There are no data available for carcinogenicity of OCBC.

As for the reproductive/developmental toxicity, no effect of OCBC on any reproductive and developmental parameters was observed in the above-mentioned combined repeat dose toxicity study in rats at doses up to 50 mg/kg bw/day. Thus the NOAEL for reproductive/developmental toxicity was considered to be 50 mg/kg bw/day in rats.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

The aquatic toxicity of *o*-chlorobenzyl chloride (OCBC) is summarized in Table 4. In each study, OCBC in the test solutions was measured except for two studies (Clariant GmbH, 1988, Dupont Chem., 1992). All the studies except one study (Dupont chem., 1992) were conducted according to OECD test guidelines in compliance with GLP. However, these studies were considered reliable with restrictions because solvents and/or dispersants were used in the studies.

Acute Toxicity Test Results

Algae

There is one study with fresh water algae, *Selenastrum capricornutum*, which was conducted in a static system according to OECD TG 201 in compliance with GLP (EA, Japan, 1999a). The 72-hr EC_{50} obtained on the basis of biomass and growth rate were 0.78 and 1.2 mg/l, respectively.

Invertebrates

One acute toxicity study with *Daphnia magna* has been reported (EA, Japan, 1999b). This study was conducted in a flow-through system according to OECD TG 202 in compliance with GLP. The 48-hr EC_{50} based on immobilization was 0.38 mg/l.

Fish

There are three studies available on acute toxicity to fish. These studies except one study (Dupont chem., 1992) were conducted according to OECD TG 203 in compliance with GLP.

One study was conducted with *Oryzias latipes* in a flow-through system and showed that the 96-hr LC_{50} was 0.27 mg/l (EA, Japan, 1999d).

The other studies were conducted with *Danio rerio* (Clariant GmbH, 1988) and with *Pimephales promelas* (Dupont Chem., 1992) in a static system and showed that the 96-hr LC_{50} were 0.5-0.71 mg/l (nominal) and 0.71-0.96 mg/l (nominal), respectively.

Chronic Toxicity Test Results

Algae

A study with fresh water algae, *Selenastrum capricornutum*, was performed in a static system according to OECD TG 201 in compliance with GLP (EA, Japan, 1999a). The 72-hr NOEC based on the biomass and growth rate were 0.045 and 0.18 mg/l, respectively.

Invertebrates

The effect of 21-day exposure on reproduction of *Daphnia magna* was investigated as a chronic study, which was conducted in a semi-static system according to OECD TG 211. This study was

well controlled under GLP regulation (EA, Japan, 1999c). The 21-day NOEC in this study was 0.020 mg/l.

Toxicity of the hydrolysis products

Based on the stability of OCBC in water (half-life, 33.1 hours at pH7), considerable hydrolysis of OCBC to *o*-chlorobenzyl alcohol is anticipated. Thus the aquatic effect of *o*-chlorobenzyl alcohol was taken into consideration. Although no toxicity data is available for this substance, the analysis by ECOSAR (ECOWIN v0.99g) showed 96-hr LC_{50} of 15.7-189.7 mg/l for fish and 48-hr LC_{50} of 0.3-0.6 mg/l for Daphnia, suggesting that *o*-chlorobenzyl alcohol is not more toxic to aquatic organisms than OCBC. Consistent with this prediction, the 96 hr LC_{50} values (nominal) of OCBC for fish obtained in a static system (0.5-0.71 mg/l for *Danio rerio* and 0.71-0.96 mg/l for *Pimephales promelas*) were larger than that obtained in a flow-through system (0.27 mg/l for *Oryzias latipes*).

Toxicity to Microorganisms

No toxicity data on aquatic microorganisms are available.

Table 4. Summary of toxicity test results to aquatic organisms.

Species	Age/Size	Stat/ Flow	Temp (°C)	Dissolved oxygen (mg/l)	Hardness (mg $CaCO_3$/l)	pH	Solvent/ dispersant	Endpoint	Concentration (mg/l)	Test method	Reference
Algae											
Selenastrum capricornutum[a)]	$1x10^4$ cells/ml (Initial cell number)	Static	23±2			7.9-8.0 (beginning) 8.0-10.5 (end)	Polyoxyethyle nesorbitan fatty acid ester, 10 mg/l	72h EC_{50} 72h NOEC biomass 24-72h EC_{50} 24-72h NOEC growth rate	0.78 [c)] 0.045 [c)] 1.2 [c)] 0.18 [c)]	OECD 201 GLP	EA, Japan, 1999a
Invertebrates											
Daphnia magna	< 24 h old	Flow-through	20±1	8.6-9	75	7.6-7.8	mixture of DMSO[b)] and polyoxyethyle nesorbitan fatty acid ester, 100 ul/l	48h EC_{50} immobilization	0.38 [c)]	OECD 202 GLP	EA, Japan, 1999b
	< 24 h old	Semi-static	20±1	8.4-9.8	87-88	7.8-8.7	Polyoxyethyle nesorbitan fatty acid ester, 0.22 mg/l	21d NOEC 21d LOEC reproduction	0.020 [c)] 0.041 [c)]	OECD 211 GLP	EA, Japan, 1999c
Fish											
Oryzias latipes	2.2 cm 0.16 g	Flow-through	24±2	8.5-9.1	45	7.1-7.4	mixture of DMSO [b)] and polyoxyethyle nesorbitan fatty acid ester, 100 ul/l	96 h LC_{50} NOEC behaviour	0.27 [c)] 0.18 [c)]	OECD 203 GLP	EA, Japan, 1999d
Danio rerio	2.8 cm	Static	21.0-23.0	6.0-9.6		7.3-8.1	Tween80, 100 ul/l	96 h LC_{50}	0.5-0.71 [d)]	OECD 203 GLP	Clariant GmbH, 1988
Pimephales promelas	2.2 cm, 0.17g	Static	22	8.3-8.4 (beginning) 2.4-7.3 (end)	72	7 (beginning) 6.2-6.9 (end)	Acetone, 0.2%	96 h LC_{50}	0.71-0.96 [d)]	Other	Dupont chem., 1992

a) now *Pseudokircheneriella subcapitata* b) dimethylsulfoxide c) Analytical monitoring was conducted. d) nominal concentration

4.2 Terrestrial Effects

No toxicity data on terrestrial organisms are available.

4.3 Other Environmental Effects

No other environmental effects data are available.

4.4 Initial Assessment for the Environment

OCBC has a water solubility of 100 mg/l at 25°C, a vapour pressure of 0.2 hPa at 25°C and a Log P_{OW} of 3.32. The K_{OC} of 856 indicates a moderate potential of the substance for adsorption to soil and sediment. The half life of OCBC by the reaction with OH radicals in air was calculated to be 103 hr. The bioconcentration factor for OCBC was calculated to be 71.85, indicating that the bioaccumulation potential of the substance is low. In the biodegradation test [OECD TG 301C], OCBC is not readily biodegradable (BOD 0% after 28 days). OCBC is hydrolyzed in water via an abiotic process to generate *o*-chlorobenzyl alcohol, which is then slowly biotransformed by oxidation to *o*-chlorobenzoic acid via *o*-chlorobenzaldehyde. An inherent biodegradability test [OECD TG 302B] showed that OCBC is inherently biodegradable with adapted industrial sludge.

The distribution of OCBC released into a particular environmental compartment was estimated with a fugacity-based model, Mackay level III. The model predicted that OCBC released into water is distributed to water (73.5 %), air (12.2%), sediment (7.7%) and soil (6.6%) while the substance released into air is distributed mainly to air (64.1%) and soil (34.6%). Almost all of the substance (99.8%) released into soil, on the other hand, was predicted to remain in its original compartment.

Acute toxicity studies with algae, invertebrates including Daphnia, and fish have been reported. The results obtained from these studies are the 72-hr EC_{50} of 0.78 mg/l for *Selenastrum capricornutum*, the 48-hr EC_{50} of 0.38 mg/l for *Daphnia magna*, and the 96-hr LC_{50} of 0.27 mg/l for *Oryzias latipes*.

A chronic toxicity test was performed to *Daphnia magna*. The 21-day NOEC for its reproduction was 0.020 mg/l (measured). The 72-hr NOEC (biomass) for the growth of *Selenastrum capricornutum* was 0.045 mg/l. No chronic toxicity data on fish are available.

Based on the stability of OCBC in water (half-life, 33.1 hours at pH7), considerable hydrolysis of OCBC to *o*-chlorobenzyl alcohol is anticipated. Thus the aquatic effect of *o*-chlorobenzyl alcohol was taken into consideration. Although no toxicity data is available for this substance, the analysis by ECOSAR (ECOWIN v0.99g) showed 96-hr LC_{50} of 15.7-189.7 mg/l for fish and 48-hr LC_{50} of 0.3-0.6 mg/l for Daphnia, suggesting that *o*-chlorobenzyl alcohol is not more toxic to aquatic organisms than OCBC. Consistent with this prediction, the 96 hr LC_{50} values (nominal) of OCBC for fish obtained in a static system (0.5-0.71 mg/l for *Danio rerio* and 0.71-0.96 mg/l for *Pimephales promelas*) were larger than that obtained in a flow-through system (0.27 mg/l for *Oryzias latipes*).

OCBC is produced by chlorination of *o*-chlorotoluene in a closed system. There is no process that generates the waste water in the production of OCBC. The waste residue is incinerated. The off-gas of the reaction is incinerated or treated on active carbon. Therefore, there is no release of OCBC to the environment from its manufacturing plants. The use pattern of OCBC is also limited to the intermediates for the production of agrochemicals. In the sponsor country, only one agrochemical is manufactured from OCBC in a closed system. Because OCBC is reacted away in the process, there is no release of OCBC from the production site of the agrochemical. No contamination of OCBC is detected in the agrochemical (detection limit 0.002%). OCBC is not detected in soil as degradation

products of agrochemicals. Based on these facts, it is considered that the impact of OCBC to the environment (aquatic and terrestrial) is negligible.

5 RECOMMENDATIONS

The chemical is currently of low priority for further work.

The chemical possesses properties indicating a hazard for human health (repeated dose toxicity) and the environment. Based on data presented by the Sponsor country, exposure to humans and the environment is anticipated to be low, and therefore this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by Sponsor countries.

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I U C L I D

D a t a S e t

Existing Chemical	ID: 611-19-8
CAS No.	611-19-8
EINECS Name	alpha,2-dichlorotoluene
EC No.	210-258-8
Molecular Formula	C7H6Cl2

Producer Related Part	
Company:	IHARA CHEMICAL INDUSTRY CO., LTD
Creation date:	16-JUL-2002
Substance Related Part	
Company:	IHARA CHEMICAL INDUSTRY CO., LTD
Creation date:	16-JUL-2002
Memo:	OECD HPV Chemicals Programme, SIDS Dossier, approved at SIAM 17 (11-14 November 2003)

Printing date:	25-NOV-2004
Revision date:	
Date of last Update:	25-NOV-2004

Number of Pages:	102

Chapter (profile):	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile):	Reliability: without reliability, 1, 2, 3, 4
Flags (profile):	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 Applicant and Company Information

Type: lead organisation
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Town: 110-0008 1-Chome, Taito-ku, Tokyo
Country: Japan
Phone: +81 3 3822 5235
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22-JAN-2004

Type: cooperating company
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Street: Stroofstrase 27
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Telefax: +49 (0) 69 3800 2707

22-JAN-2004

Type: cooperating company
Name: Tessenderlo Chemie N.V.
Street: Rue du Trone n 130
Town: 3980 B-1050 Brussels
Country: Belgium
Phone: +32 2 639 18 11
Telefax: +32 2 639 19 99
Telex: 23619 prolimb

28-JAN-2004

1.0.2 Location of Production Site, Importer or Formulator
-

1.0.3 Identity of Recipients
-

1.0.4 Details on Category/Template
-

1.1.0 Substance Identification
-

1.1.1 General Substance Information

Substance type: organic
Physical status: liquid
Purity: > 99 - % w/w

22-JAN-2004

1.1.2 Spectra
-

1.2 Synonyms and Tradenames

o-Chlorobenzyl chloride

22-JAN-2004

alpha, 2-Dichlorotoluene

22-JAN-2004

alpha, o-Dichlorotoluene

22-JAN-2004

1-Chloro-2-(chloromethyl)benzene

22-JAN-2004

2-Chlorobenzyl chloride

22-JAN-2004

o, alpha-Dichlorotoluene

22-JAN-2004

Benzene, 1-chloro-2-(chloromethyl)-

22-JAN-2004

Toluene, o, alpha-dichloro-

22-JAN-2004

alpha, 2-Dichlortoluol

22-JAN-2004

alpha-2-diclorotolueno

22-JAN-2004

1.3 Impurities

CAS-No: 89-98-5
EC-No: 201-956-3
EINECS-Name: 2-chlorobenzaldehyde
Contents: = .014 - % w/w

Remark: 0.01-0.02% w/w
22-JAN-2004

CAS-No: 104-83-6
EC-No: 203-242-7

EINECS-Name: alpha,4-dichlorotoluene
Contents: = .229 - % w/w

Remark: 0.18-0.26% w/w
22-JAN-2004

CAS-No: 88-66-4
EC-No: 201-849-1
EINECS-Name: 1-chloro-2-(dichloromethyl)benzene
Contents: = .063 - % w/w

Remark: 0.04-0.08% w/w
22-JAN-2004

1.4 Additives
-

1.5 Total Quantity

Remark: The production quantity of o-chlorobenzyl chloride (OCBC) in Germany, Japan and Belgium is reported as follows

Annual production (tonnes)

Year	Germany	Japan	Belgium
1999	140	156	0
2000	700	390	0
2001	350	431	653
2002	180	330	552
2003	-	149	-

-: No data available
In these countries, only one company, which has one production site, currently operates the production of OCBC.

30-JUL-2004 (11) (25) (35)

1.6.1 Labelling

Labelling: provisionally by manufacturer/importer
Symbols: (Xn) harmful
(N) dangerous for the environment
R-Phrases: (20/21/22) Harmful by inhalation, in contact with skin and if swallowed
(36/37/38) Irritating to eyes, respiratory system and skin
(50/53) Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment

29-JAN-2004

1.6.2 Classification

Classified: provisionally by manufacturer/importer

Class of danger: harmful

Remark: Classification :EC-classification, provisionally by manufacturer
Class of danger :Harmful, Irritant, Dangerous for environment
R-Phrases:
R20/21/22
Harmful by inhalation, in contact with skin and if swallowed.
R36/37/38
Irritating to eyes, respiratory system and skin.
R50/53
Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
30-JUL-2004

1.6.3 Packaging
-

1.7 Use Pattern

Type: industrial
Category: other

Remark: intermediate for the production of agrochemicals
22-JAN-2004

1.7.1 Detailed Use Pattern
-

1.7.2 Methods of Manufacture
-

1.8 Regulatory Measures
-

1.8.1 Occupational Exposure Limit Values

Remark: No data available
16-JUL-2002

1.8.2 Acceptable Residues Levels
-

1.8.3 Water Pollution

Remark: Classified by :Germany: Federal Water Act on the Classification of Water-Endangering Substances in

Water-Endangering Classes (WGK)
Labelled by :
Class of danger :3 (severely water-endangering)
Remark :Classification according to VwVwS, Annex 3
WGK Identification Number:4459
30-JUL-2004

1.8.4 Major Accident Hazards
-

1.8.5 Air Pollution
-

1.8.6 Listings e.g. Chemical Inventories
-

1.9.1 Degradation/Transformation Products
-

1.9.2 Components
-

1.10 Source of Exposure

Remark: Occupational exposure monitoring was conducted at the production site in Japan.

-Date: 2003/01/14-Method:Air of workplace atmosphere (around the mouth of workers) was aspirated by suction pump at flow rates of 0.2 l/min for 2-21 minutes, and extracted with carbon disulfide, and analyzed by GC-FID.

-Result
Table 1.Concentration of o-chlorobenzyl chloride (OCBC) in the air of workplace atmosphere

Work Process*	Number of samples	Working time	Mean Concentration (ppm) (Min-Max)
(1)	2	10 sec./3days	ND (< 0.013)
(2)	4	10 sec./day	ND (<0.017)
(3)	8	20 min./day	0.0153 (<0.005-<0.025)
(4)	2	6.5 hrs./day 3 min./drum	0.008 (0.004-0.012)
(5)	2	5 min./day	ND (<0.013)

*: Work Process
(1) Putting stabilizer in a tank
(2) Putting raw material in a tank
(3) Sampling and preparation for GC-FID analysis
(4) Filling a drum
(5) Treatment of waste oil (residual)

Production site
30-JUL-2004 (25)

Remark: Production site
The number of operation days at the production site is follows;
In Japan: 2-6 weeks/year in 1999-2003
In Germany: 3-24 weeks/year
28-JAN-2004 (11) (25)

Remark: In Japan, Germany and Belgium, the number of workers engaged in manufacturing and processing is limited to less than twenty.
Production site
22-JAN-2004 (11) (25) (35)

Remark: At the user site in the sponsor country, OCBC is used as the intermediate for the production of the agrochemical in a closed system and treated in a way similar to that at the production site. Putting OCBC into a reaction tank is the only process that might cause occupational exposure at the user site because OCBC is reacted away in the production of the agrochemical and no contamination of OCBC is detected in the final product (detection limit 0.002%). This process is just like a reverse process of filling drum with OCBC at the production site. Thus the OCBC concentrations in the air of workplace atmospheres at the user site are anticipated to be at the same level or less at the production site. Furthermore, workers at the user site are also obliged to use personal protection equipments such as mask, safety glasses and gloves during operation. Based on these facts, occupational exposure situation at the user site is equal or less compared to the situation at the production site in the sponsor country. Therefore the occupational exposure to OCBC is also considered to be negligible in the sponsor country.
User site
29-JAN-2004 (25)

Remark: OCBC is produced by chlorination of o-chlorotoluene in a closed system. There is no process that generates the waste water in the production of OCBC. The waste residue is incinerated. The off-gas of the reaction is incinerated or treated on active carbon. Therefore there is no release of OCBC to the environment from its manufacturing plants.

In the sponsor country, there is only one user site, which is located near the production site. At this site, only one agrochemical is manufactured from OCBC in a closed system. Because OCBC is reacted away in the process, there is no release of OCBC to the environment from the production site of the agrochemical.

The use of agrochemicals manufactured from OCBC might be the source of environmental exposure of OCBC. This exposure scenario is not expected in the sponsor country, however,

because no contamination of OCBC is detected in the final products (detection limit 0.002%) and OCBC is not detected as degradation products of agrochemicals in soil.
Source of environmental exposure
28-JAN-2004 (11) (19) (25) (35)

Remark: Source of consumer exposure
The use of OCBC is limited to intermediates for producing agrochemicals. The agrochemicals manufactured from OCBC are only two herbicides in OECD countries. In the sponsor country, only one herbicide is produced and used. No contamination of OCBC is detected in this herbicide by GC analysis (detection limit 0.002%). Therefore, consumer exposure is considered negligible in the sponsor country.
28-JAN-2004 (11) (25) (35)

1.11 Additional Remarks
-

1.12 Last Literature Search

Date of Search: 17-JUL-2003

Remark: ACGIH
Aquire
ChemFinder
CHRIS
DIALO
GECDIN
HSDB
IARC
IRIS
IUCLID
MSDS
NCI
NIO
OHMTADS
RTE
STN (CA, Registry, BEIL, GMELIN, HODOC, MEDLINE, NIOSHTIC, PROMT, RTECS, SPECINFO, TOXLINE, TOXLIT)
SRC PhysPro Database
TOXLINE
TSCATS
28-JAN-2004

1.13 Reviews
-

2.1 Melting Point

Value: = -17 degree C

Reliability: (2) valid with restrictions
Data from peer reviewed secondary source
Flag: Critical study for SIDS endpoint
28-JAN-2004 (36)

Value: <= 50 degree C

Method: OECD Guide-line 102 "Melting Point/Melting Range"
Year: 1999
GLP: no

Test substance: -Source: Wako Pure Chemical Industries, Ltd.
-Lot No.LEM4431
-Purity: 99.6%
Reliability: (2) valid with restrictions
OECD Guideline study
28-JAN-2004 (3)

2.2 Boiling Point

Value: = 217 degree C at 1013 hPa

Reliability: (2) valid with restrictions
Data from peer reviewed secondary source
Flag: Critical study for SIDS endpoint
28-JAN-2004 (36)

Value: = 94 - 95 degree C at 13.3 hPa

Reliability: (2) valid with restrictions
Data from peer reviewed secondary source
28-JAN-2004 (36)

Value: = 96.6 degree C at 20 hPa

Reliability: (2) valid with restrictions
Data from peer reviewed secondary source
28-JAN-2004 (20)

2.3 Density

Type: density
Value: = 1.2743 g/cm³ at 20 degree C

Reliability: (2) valid with restrictions
Data from peer reviewed secondary source
Flag: Critical study for SIDS endpoint
22-JAN-2004 (20)

Type: relative density
Value: = 1.2699 at 0 degree C

Reliability: (2) valid with restrictions
Data from peer reviewed secondary source
Flag: Critical study for SIDS endpoint
28-JAN-2004 (36)

2.3.1 Granulometry
-

2.4 Vapour Pressure

Value: = .2 hPa at 25 degree C

Method: other (calculated)
Year: 2002

Method: MPBPWIN V1.40
Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
28-JAN-2004 (5)

2.5 Partition Coefficient

log Pow: = 3.32 at 25 degree C

Method: OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
Year: 1999
GLP: yes

Method: Three different solvent ratios were investigated. A volume ratio of n-octanol to water and a quantity of test substance are as follows:

Test condition No.	(1)	(2)	(3)
n-Octanol phase saturated with water(ml)	5	10	20
Water phase saturated with n-octanol(ml)	30	25	15
Test substance(mg)	5.05	5.05	5.05

All tests were performed in duplicate. After the partition equilibrium of test substance was established between n-octanol and water phases at three volume ratios, the concentrations of test substance in both phases were determined by HPLC (high performance liquid chromatography). And a pH of water phases was measured.

Result: Partition Coefficient of o-chlorobenzyl chloride (OCBC) under three conditions at 25 degC (g/L):

Test Condition No.	Pow (Cn-octanol/Cwater)	Log Pow Mean	pH (water phase)

1	a	2.07E+3	3.32	3.32	6.4
	b	2.14E+3	3.33		
2	a	2.08E+3	3.32	3.32	6.4
	b	2.12E+3	3.33		
3	a	1.96E+3	3.29	3.30	6.4
	b	2.07E+3	3.32		
Mean		2.07E+3	3.32		6.4

Test substance: -Source: Wako Pure Chemical Industries, Ltd.
-Lot No.LEM4431
-Purity: 99.6 % (but treated as 100 %)
Reliability: (1) valid without restriction
OECD Guideline study
Flag: Critical study for SIDS endpoint
29-JAN-2004 (4)

log Pow: = 3.44

Method: other (calculated)

Method: KOWWIN V1.66
Reliability: (2) valid with restrictions
28-JAN-2004 (5)

2.6.1 Solubility in different media

Solubility in: Water
Value: = 100 mg/l at 25 degree C

Method: OECD Guide-line 105
Year: 1999
Test substance: other TS

Method: After shaking vessels for 24, 48 and 72 hours at 30+/-1 deg C, these were shaken for 24 hours at 25+/-1 deg C. The concentrations of the test substance in the clear aqueous phase were determined by HPLC analysis.
Result: Concentration of o-chlorobenzyl chloride (OCBC) measured at 25 deg C (mg/L):

Shaking time(hr)	Concentration of substance	Mean	Mean
24	110	110	
	110		
48	110	100	100
	100		(C.V.4.5%)
72	100	100	
	100		

C.V.: coefficient of variation
Test substance: -Source: Wako Pure Chemical Industries, Ltd.
-Lot No.LEM4431

-Purity: 99.6 %
Reliability: (2) valid with restrictions
OECD Guideline study
Flag: Critical study for SIDS endpoint
25-NOV-2004 (3)

2.6.2 Surface Tension
-

2.7 Flash Point

Value: = 114 degree C
Type: open cup

Reliability: (2) valid with restrictions
28-JAN-2004 (25)

2.8 Auto Flammability

Value: = 634 degree C

Reliability: (2) valid with restrictions
28-JAN-2004 (25)

2.9 Flammability
-

2.10 Explosive Properties

Result: other

Remark: Range of explosion is 2.0 - 8.6 %.
Result: o-Chlorobenzyl chloride has explosive nature.
Reliability: (4) not assignable
28-JAN-2004 (25)

2.11 Oxidizing Properties
-

2.12 Dissociation Constant
-

2.13 Viscosity
-

2.14 Additional Remarks

Remark: o-Chlorobenzyl chloride (OCBC) is a clear, colorless, liquid and has pungent odor.
29-JAN-2004

3.1.1 Photodegradation

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 1500000 molecule/cm³
Rate constant: = .0000000000012454 cm³/(molecule * sec)
Degradation: = 50 % after 103 hour(s)

Method: other (calculated)
Year: 2002

Method: AOPWIN Ver.1.90
Remark: The length of the day: 12hr/day
Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
28-JAN-2004 (5)

3.1.2 Stability in Water

Type: abiotic
t1/2 pH4: = 34.9 hour(s) at 25 degree C
t1/2 pH7: = 33.1 hour(s) at 25 degree C
t1/2 pH9: = 36.4 hour(s) at 25 degree C

Method: OECD Guide-line 111 "Hydrolysis as a Function of pH"
Year: 1999
Test substance: other TS

Method: Test were conducted at three (4, 7, 9) pHs at two (30+/-1 deg C, 40+/-1 deg C) temperatures. All tests were performed in duplicate.

In each pHs and each temperatures, the logarithm of concentration (logC) were plotted against time (t), and a slope(a) and an intercept(b) were derived from following regression equation.
logC = at + b
A rate constant (k) and a half-life time (t1/2) were derived from following equation.
k = -2.303 X a
t1/2 =0.693/k
Then, in each pHs, the logarithm of a rate constant (logk) were plotted against the reciprocal absolute temperature (1/T), and regression equation was derived by least-squares method. The rate constant and half-life time at 25 deg C were derived by extrapolation method.

Result: Half-life times of OCBC at 25 deg C:

pH	Half-life time in hours (t1/2)	Temperature in deg C	Rate constant in hours-1
pH4	34.9	25	1.99E-2
pH7	33.1	25	2.1E-2
pH9	36.4	25	1.90E-2

The o-chlorobenzyl chloride (OCBC) is hydrolyzed at pH 4.0, 7.0 and 9.0. (not stable in water)

Test substance: -Source: Wako Pure Chemical Industries,Ltd.
-Lot No.LEM4431
-Purity: 99.6 %
Reliability: (2) valid with restrictions
OECD Guideline study
Flag: Critical study for SIDS endpoint
30-JUL-2004 (3)

3.1.3 Stability in Soil

Remark: No data available for stability in soil of o-chlorobenzyl chloride (OCBC). But, the data for stability in soil of an agrochemical manufactured from OCBC is available. OCBC is not detected as degradation products of agrochemicals in soil (see 3.8).
28-JAN-2004 (19) (27)

3.2.1 Monitoring Data (Environment)

Remark: No data available
16-JUL-2002

3.2.2 Field Studies
-

3.3.1 Transport between Environmental Compartments

Type: fugacity model level III
Media: other:Air-sediment-soil-water
Year: 2002

Result:

Compartment	Release		
	100%to air	100%to water	100%to soil
Air	64.1%	12.2%	0.2%
Water	1.1%	73.5%	0.0%
Soil	34.6%	6.6%	99.8%
Sediment	0.1%	7.7%	0.0%

The detailed results and the input parameters used in the calculation are shown in Appendix 1.
The reference of the Fugacity model Level III is "D. Mackay, S. Paterson, W. Y. Shiu, Generic Models for Evaluating The Regional Fate of Chemicals, Chemosphere, 24, 6, 695-717. (1992)"
Attached doc.: Appendix1.doc:The parameters used in the fugacity calculation (Level III)
Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint

24-NOV-2004 (5)

3.3.2 Distribution

Remark: Henry's law constant of o-chlorobenzyl chloride is estimated at 157 Pa m3/mole (bond estimation method) by HENRYWIN v3.10.
The input parameters are following;
CAS No. 611-19-8
SMILES: c(c(cccl)CL)(cl)CCL
Water solubility: 100 mg/l
Log KOW: 3.32
Boiling point: 217 deg C
Melting point: -17 deg C
18-FEB-2004 (5)

Remark: The soil adsorption coefficient (KOC) of o-chlorobenzyl chloride is estimated as 856 by PCKOCWIN v1.66.
The input parameters are following;
CAS No. 611-19-8
SMILES: c(c(cccl)CL)(cl)CCL
Water solubility: 100 mg/l
Log KOW: 3.32
Boiling point: 217 deg C
Melting point: -17 deg C
28-JAN-2004 (5)

3.4 Mode of Degradation in Actual Use
-

3.5 Biodegradation

Type: aerobic
Inoculum: activated sludge
Concentration: 100 mg/l related to Test substance
Contact time: 28 day(s)
Degradation: = 0 % after 28 day(s)
Result: under test conditions no biodegradation observed
Control Subst.: Aniline
Kinetic: 7 day(s) = 68 %
14 day(s) = 74 %
Deg. product: yes

Method: OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"
Year: 1998
GLP: yes

Method: -Inoculum
1.Fresh sludge samples were collected from ten sites in Japan, such as municipal sewage-treatment plants, rivers, lakes and seas.

The filtered supernatant of an activated sludge (cultivated sludge for 3 months) were mixed with an equal volume of the

filtered supernatant of freshly collected ten-source mixture when used. And the activated sludge were cultivated for OECD TG 301C.

-Method
Thirty mg of the test substance or aniline (reference substance) and 9 mg as MLSS (mixed liquor suspended solid) of activated sludge were added to 300 ml of test medium (OECD TG 301C). A concentration of inoculum was 30 mg/l as MLSS. A concentration of the test substance was 100 mg/l. A volume of mixture was 300 ml. The test and reference solutions were cultivated in BOD meter together with the inoculum blank and abiotic control ones at 25 deg C for 28 days, during which the oxygen consumption was continuously measured. After termination of the test, the residual amount of the test substance and DOC (dissolved organic carbon) were determined individually with HPLC and TOC meter. And pH values of test solutions were measured. The biodegradability was calculated from the oxygen consumption and the residual amount.

Result: Results of test substance and specific chemical analysis by HPLC at end of test (after 28 days) are as follows:

	Residual amount of test substance	Breakdown products		
		o-chlorobenzyl alcohol	o-chlorobenz aldehyde	o-chlorobenzoic acid
[Water + test substance solutions]				
mg	0	26.3	0	0
%	0	99	0	0
[Sludge + test substance solutions (Value are expressed as mean of three times)]				
mg	0	24.5	0.7	0.9
%	0	92	2	3
[Theoretical Value]				
mg	30.0	26.6	26.2	29.2

Results of carbon analysis by TOC and of BOD at end of test (after 28 days) are as follows:

	Water+test substance Solutions	Sludge+test substance solutions
[Residual amount of DOC]		
mgC	15.8	16
(Theoretical Value 15.7 mgC)		
%	100	102
[BOD]		
mg	0	0

o-Chlorobenzyl chloride (OCBC) was not detected at both water plus test substance and sludge plus test substance solutions after 28 days. In water plus test substance solutions, o-chlorobenzyl alcohol was detected by LC-MS

after 28 days. Production rate of o-chlorobenzyl alcohol was 99 % from the measurement by HPLC. Therefore, it is considered that OCBC hydrolyzed into o-chlorobenzyl alcohol. In sludge plus test substance solutions, o-chlorobenzyl alcohol, o-chlorobenzaldehyde and o-chlorobenzoic acid were detected respectively after 28 days. Mean production rates of o-chlorobenzyl alcohol, o-chlorobenzaldehyde and o-chlorobenzoic acid were 92, 2 and 3 % respectively. Consequently it is considered that OCBC is hydrolyzed and produces o-chlorobenzyl alcohol, and then the o-chlorobenzyl alcohol is slowly biodegradable to o-chlorobenzaldehyde and o-chlorobenzoic acid. Degradation pathway of o-chlorobenzyl chloride is as follows:
o-chlorobenzyl alcohol, o-chlorobenzaldehyde, o-chlorobenzoic acid

Conclusion: In this test, the determination by the BOD method showed 0% degradation of OCBC through 28 days

Reliability: (1) valid without restriction
OECD Guideline study

Flag: Critical study for SIDS endpoint

30-JUL-2004 (2)

Type: aerobic
Inoculum: activated sludge, industrial, adapted
Concentration: 50 mg/l related to COD (Chemical Oxygen Demand)
Contact time: 28 day(s)
Degradation: = 99 % after 9 day(s)
Result: other:Under this test conditions OCBC is inherently biodegradable.(99 % after 9 days with adaptation period of 6 days)

Method: OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year: 1990
GLP: no

Remark: A mixture containing OCBC, mineral nutrients and an industrial activated sludge was agitated with aeration. This test was adapted to the volatility of a test substance by using a respirometric method to determine the biodegradation instead of DOC measurement. Thus the result was not influenced by volatilisation if any. The determination by the respirometric method showed 99% degradation of OCBC after 9 days. First 6 days were adaptation period (less than 10% degradation) and 90% degradation of OCBC was observed in the last 3 days. Thus, OCBC is inherently biodegradable with adapted industrial sludge.

Reliability: (2) valid with restrictions

28-JAN-2004 (38)

3.6 BOD5, COD or BOD5/COD Ratio

-

3.7 Bioaccumulation

BCF: = 71.85

Method: other:(calculated), BCFWIN V 2.14

Remark: logKow=3.32 (measured)
Reliability: (2) valid with restrictions
28-JAN-2004 (5)

3.8 Additional Remarks

Remark: [Degradation of Orbencarb]
The degradation of 14C-orbencarb, an agrochemical manufactured from OCBC, was studied under various soil conditions, and three types of soils were used. Under upland conditions, 14CO2 evolved rapidly in soil, where the half-lives of orbencarb were 18 to 26 days. Orbencarb sulfoxide, monodesethyl-orbencarb, methyl 2-chlorobenzylsulfoxide, methyl 2-chlorobenzyl-sulfone and 2-chlorobenzylsulfonic acid were identified as orbencarb's major degradation products and N-ethyl-N-vinyl-orbencarb, N-ethyl-N-beta-hydroxyethyl-orbencarb, 4-hydroxy-orbencarb, 5-hydroxy-orbencarb, didesethyl-orbencarb, 2-chlorobenzyl alcohol, 2-chlorobenzoic acid and methyl 2-chlorobenzylsulfide as its minor. Soil bound residues derived from its 14C-U-benzen ring were found in humic acid, hulvic acid and humin fractions, and its benzene ring was finally degraded to 14 CO2.
28-JAN-2004 (27)

Remark: OCBC is not formed during any known mechanism of degradation of clomazone in soil. Clomazone is an agrochemical manufactured from OCBC.
28-JAN-2004 (19)

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type:	flow through
Species:	Oryzias latipes (Fish, fresh water)
Exposure period:	96 hour(s)
Unit:	mg/l Analytical monitoring: yes
LC50:	= .27 -
Method:	OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year:	1999
GLP:	yes
Test substance:	other TS:Wako Pure Chemical Industries, Ltd., Purity 99.6 %, Lot No. PAM5243

Method:

[Test Organisms]
a) Size (length and weight): 2.2 cm (2.1 - 2.4 cm) in length; 0.16 g (0.11 - 0.20 g) in weight
b) Age: Not described
c) Pretreatment: Acclimated for seven days or more and not fed for 24hours prior to the test. Any groups showing > 5 % mortality in the acclimation period were not used for the test.
d) Supplier/Source: Takizawa Fish Hatchery, Ltd.

[Test Conditions]
a) Dilution Water Source: Laboratory supply water (dechlorinated)
b) Dilution Water Chemistry:
Hardness : 45 mg/l (as CaCO3)
PH : 7.6
c) Exposure Vessel Type: 9-liter test solution in a 10-liter glass vessel.
d) Nominal Concentrations (mg/l): 0, 0.10, 0.18, 0.32, 0.56 and 1.0
e) Solvent/Dispersant and Concentrations: Mixture of dimethylsulfoxide and polyoxyethylenesorbitan fatty acid ester,100 ul/l test solution
f) Stock Solutions and Stability: 1, 1.8, 3.2, 5.6 and 10 mg/ml solvent
g) Number of Replicates: 1
h) Fish per Replicates: 10
i) Renewal Rate of Test Water: Flow-through with a flow-rate of 50 ml/min, comparable to 8-times renewal per day
J) Water Temperature: 23.2 - 23.9 deg C
k) Light Condition: 16:8 hours, light-darkness cycle
l) Aeration: No
m) Feeding: No

[Analytical Procedure]
Portions of the test solutions were withdrawn at 0 hour and 48 hours and extracted with hexane. Concentrations of the test substance were determined by gas chromatography.

[Statistical Method]
a) Data Analysis: Binominal method for LC50
b) Measured Concentrations : Geometric mean concentrations

Result:

[Measured Concentrations]
All of the measured concentrations were between 80 and 120%

of the nominal concentrations (Table 1). Thus the nominal concentrations were used for calculating effect values.

Table 1.Measured concentrations of the test solutions in the 96-hour acute toxicity test on Oryzias latipes under the flow-through test conditions

Nominal concn.	Measured concn. (mg/l)		Arithmetic mean	Measured/Nominal (%)	
(mg/l)	0 h	48 h	(mg/l)	0 h	48h
Control	< 0.005	< 0.005	---	---	---
Solv. cont.	< 0.005	< 0.005	---	---	---
0.10	0.100	0.101	0.101	100	101
0.18	0.158	0.183	0.171	88	102
0.32	0.368	0.287	0.328	115	90
0.56	0.543	0.513	0.528	97	92
1.0	0.971	1.05	1.01	97	105

[Water Chemistry]
Table 2.pH values of the test solutions in the 96-hour acute toxicity test on Oryzias latipes under the flow-through test coditions

	Cont.	Solv.	Nominal concn. (mg/l)				
Hours		cont.	0.10	0.18	0.32	0.56	1.0
0	7.2	7.2	7.2	7.2	7.2	7.2	7.2
24	7.4	7.3	7.3	7.3	7.3	7.3	7.2
48	7.3	7.3	7.3	7.2	7.2	7.2	7.2
72	7.2	7.2	7.2	7.1	7.1	7.1	ND
96	7.3	7.3	7.3	7.3	7.3	ND	ND

ND: Not determined because all fishes were dead at this time.

Table 3.Dissolved oxygen concentrations (DO) of the test solutions in the 96-hour acute toxicity test on Oryzias latipes under the flow-through test conditions

	Cont.	Solv. cont.	Nominal concn. (mg/l)				
Hours			0.10	0.18	0.32	0.56	1.0
0	8.8	8.8	8.6	8.7	8.8	8.8	8.7
24	8.5	8.6	8.5	8.5	8.7	8.6	8.7
48	8.5	8.6	8.5	8.6	8.6	8.6	8.8
72	9.0	8.9	8.9	8.9	8.9	9.1	ND
96	8.7	8.9	8.6	8.6	8.8	ND	ND

ND: Not determined because all fishes were dead at this time.

[Effect Data]
LC50 (96 hr) : 0.27 mg/l(Table 4 & 5)

LC0 (96 hr) : 0.18 mg/l(Table 4 & 6)
LC100 (96 hr) : 0.56 mg/l(Table 4 & 6)
NOEC (96 hr) : 0.18 mg/l(Table 4 & 7)

Table 4.Cumulative numbers of deaths in the 96-hour acute toxicity test on Oryzias latipes under the flow-through test conditions

Nominal concn.	Cumulative number of deaths(a)			
(mg/l)	24hr	48hr	72hr	96hr
Control	0 (0)	0 (0)	0 (0)	0 (0)
Solv. Control	0 (0)	0 (0)	0 (0)	0 (0)
0.10	0 (0)	0 (0)	0 (0)	0 (0)
0.18	0 (0)	0 (0)	0 (0)	0 (0)
0.32	0 (0)	0 (0)	4 (40)	8 (80)
0.56	1 (10)	8 (80)	10 (100)	10 (100)
1.0	2 (20)	10 (100)	10 (100)	10 (100)

(a):Percentage of dead animals compared to the total animals tested is shown in parentheses.

Table 5.Calculated LC50 values based on the nominal concentrations in the 96-hour acute toxicity test on Oryzias latipes under the flow-through test conditions

Exposure Period (hours)	LC50 (mg/l)	95% confidence limit (mg/l)	Statistical method
24	> 1.0	not calculated	Binominal
48	0.47	not calculated	Binominal
72	0.34	not calculated	Binominal
96	0.27	not calculated	Binominal

Table 6.Maximum concentrations causing 0% mortality and Minimum concentrations causing 100% mortality based on the nominal concentrations in the acute toxicity test on Oryzias latipes under the flow-through test conditions

	Exposure time			
	24 hr	48 hr	72 hr	96 hr
Maximum concn. (mg/l) causing 0% mortality	0.32	0.32	0.18	0.18
Minimum concn. (mg/l) causing 100% mortality	> 1.0	1.0	0.56	0.56

Table 7.Visible abnormalities in the 96-hour acute toxicity test on Oryzias latipes under the flow-through test conditions

Nominal concn. (mg/l)	Symptom 24hr	48hr	72hr	96hr
Control	Normal	Normal	Normal	Normal
Solv. Control	Normal	Normal	Normal	Normal
0.10	Normal	Normal	Normal	Normal
0.18	Normal	Normal	Normal	Normal
0.32	Normal	le	le, ss, es	es
0.56	le, ss	le, ss	---a	---a
1.0	le, ss	---a	---a	---a

le: Lethargy
ss: Surface slicks
es: Erratic swimming
a: No observation was made because all fishes were dead at this time.

Reliability: (2) valid with restrictions
OECD TG study with use of solvent/dispersant

Flag: Critical study for SIDS endpoint

30-JUL-2004 (18)

Type: static
Species: other:Danio rerio (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = .5 - .71

Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: 1988
GLP: yes
Test substance: other TS: Purity 99.6%

Method: [Test Organisms]
a) Size (length and weight): 2.8 cm (2.4 - 3.4 cm) in length
b) Age: Not described
c) Pretreatment: Acclimated for 14 days or more
d) Supplier/Source: West Aquarium, Bad Lauterberg.

[Test Conditions]
a) Dilution Water Source: synthetic according to ISO 7346/1
b) Dilution Water Chemistry:
pH: 7.9-8.2
c) Exposure Vessel Type: 10-liter test solution
d) Nominal Concentrations (mg/l): 0, 0.25, 0.5, 0.71,1.0,1.8, 10,100
e) Dispersant and Concentrations: Tween 80, 100 ul/l test solution
f) Number of Replicates: 1
g) Fish per Replicates: 10
h) Water Temperature: 21.0 - 23.0 deg C
i) Light Condition: 12:12 hours, light-darkness cycle
j) Aeration: No
k) Feeding: No

[Statistical Method]
a) Data Analysis: Probit analysis for LC50

Result: [Effect Data]

LC50(48 hr): 1.25-1.8 mg/l
LC50(96 hr): 0.5-0.71 mg/l conf.interval:.0.59-0.8 mg/l
LC0(48 hr): 1 mg/l
LC0(96 hr): 0.5 mg/l
LC100(48 hr): 1.8 mg/l
LC100(96 hr): 1.25 mg/l

Table1.Cumulative numbers of deaths in the acute toxicity Test on Danio rerio

Nominal concn. (mg/l)	Cumulative number of deaths(a) 24hr	48hr	72hr	96hr
Control	0 (0)	0 (0)	0 (0)	0 (0)
Solv. Control	0 (0)	0 (0)	0 (0)	0 (0)
0.25	0 (0)	0 (0)	0 (0)	0 (0)
0.5	0 (0)	0 (0)	0 (0)	0 (0)
0.71	0 (0)	0 (0)	7 (70)	8 (80)
1	0 (0)	0 (0)	3 (30)	7 (70)
1.25	0 (0)	3 (30)	10 (100)	10 (100)
1.8	0 (0)	10 (100)	10 (100)	10 (100)
10	10 (100)	10 (100)	10 (100)	10 (100)
100	10 (100)	10 (100)	10 (100)	10 (100)

(a):Percentage of dead animals compared to the total animals tested is shown in parentheses.

Table2. Water parameter

Parameter	test solutions	control
pH	7.3 - 8.1	7.3 - 8.1
Dissolved oxygen	6.0 - 9.3	7.0 - 9.6
Temperature	21.0 - 23.0	21.2 - 23.0

Reliability: (2) valid with restrictions
OECD TG study with use of dispersant. The test solutions were no analysed.
30-JUL-2004 (10)

Type: static
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = .71 - .96

Method: other
Year: 1979
Test substance: other TS:Submitted by C.R. Haaf, Chemicals, Dyes & Pigments Dept., Jackson Lab.

Method: [Test Organisms]
a) Size (length and weight): 2.2 cm in length; 0.17 g in weight
b) Age: Not described
c) Pretreatment: Fasted for 48 hours prior to the test
d) Supplier/Source: Not described

[Test Conditions]
a) Dilution Water Source: Laboratory supply water
b) Dilution Water Chemistry:
Total alkalinity : 110 mg/l (as CaCO3)
Total hardness : 72 mg/l
Specific conductance : 190 umhos
c) Exposure Vessel Type: 15-liter test solution in a glass vessel
d) Nominal Concentrations (v/v, ppm): 0, 0.1, 0.15, 0.24, 0.32, 0.42, 0.56, 0.75, 1.0 and 1.5
e) Solvent and Concentrations: Acetone
f) Stock Solutions Preparations and Stability: 0.2% in acetone
g) Number of Replicates: 1
h) Fish per Replicates: 10
i) Renewal Rate of Test Water: No renewal
j) Water Temperature: 22 deg C
k) Light Condition: Not described
l) Aeration: No
m) Feeding: No

[Analytical Procedure]
The test solutions were not analysed for the test substance.

[Statistical Method]
a) Data Analysis: No analysis
b) Method of Calculating Mean Measured Concentrations: Not calculated because concentrations of the test solutions were not measured.

Result: [Water Chemistry]
Table 1.Dissolved oxygen and pH values of the test solutions measured at the beginning and the end of the test.

Nominal concn.		pH		Dissolved oxygen(ppm)	
(ppm) (v/v)	(mg/l)a)	beginning	end	beginning	end
Control		7.0	6.4	8.4	3.0
Acetone control		7.0	6.3	8.3	2.7
0.1	0.13	7.0	6.3	8.3	2.4
0.15	0.19	7.0	6.3	8.3	4.0
0.24	0.31	7.0	6.2	8.4	2.7
0.32	0.41	7.0	6.3	8.3	2.7
0.42	0.54	7.0	6.3	8.3	2.8
0.56	0.71	7.0	6.2	8.3	2.6
0.75	0.96	7.0	6.6	8.3	6.5
1.0	1.27	7.0	6.7	8.4	7.0
1.5	1.91	7.0	6.9	8.4	7.3

a): convert ppm to mg/l using 1ppm(v/v)=1ul/l=1.274mg/l (relative density=1.274).

[Effect Data]
Table 2.Percentage of deaths in the 96-hour acute toxicity test on Pimephales promelas under the static test conditions

Nominal concn	Mortality (%)

	(v/v, ppm)	(mg/l) a)
Control		0
Acetone control		0
0.1	0.13	0
0.15	0.19	0
0.24	0.31	0
0.32	0.41	0
0.42	0.54	0
0.56	0.71	20
0.75	0.96	100
1.0	1.27	100
1.5	1.91	100

a): convert ppm to mg/l using 1ppm(v/v)=1ul/l=1.274mg/l (relative density=1.274).

Reliability: (2) valid with restrictions
The test solutions were no analysed.

30-JUL-2004 (14)

4.2 Acute Toxicity to Aquatic Invertebrates

Type: flow through
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: yes
NOEC: = .1 -
EC50: = .38 -

Method: OECD Guide-line 202
Year: 1999
GLP: yes
Test substance: other TS:Wako Pure Chemical Industries, Ltd., Purity 99.6 %, Lot No. PAM5243

Method: [Test Organisms]
a) Age: < 24 hours old
b) Supplier/Source: National Institute for Environmental Studies (JAPAN)

[Test Conditions]
a) Dilution Water Source: Laboratory supply water (dechlorinated)
b) Dilution Water Chemistry:
Hardness : 75 mg/l (as CaCO3)
pH : 7.5
c) Exposure Vessel Type: 9-liter test solution in a 10-liter glass vessel
d) Nominal Concentrations (as mg/l): 0, 0.10, 0.18, 0.32, 0.56 and 1.0
e)Solvent/Dispersant and Concentrations: Mixture of dimethylsulfoxide and polyoxyethylenesorbitan fatty acid ester, 100 ul/l test solution
f) Stock Solutions and Stability: 1, 1.8, 3.2, 5.6 and 10 mg/ml solvent
g) Number of Replicates: 4
h) Individuals per Replicates: 5
i) Renewal Rate of Test Water: Flow-through with a flow-rate of 50 ml/min, equivallent to 8-times renewal per day

j) Water Temperature: 20.0 - 20.1 deg C
k) Light Condition: 16:8 hours, light-darkness cycle
l) Feeding: No

[Analytical Procedure]
Portions of the test solutions were withdrawn at 0 hour and 48 hours and extracted with hexane. Concentrations of the test substance were determined by gas chromatography.

[Statistical Method]
a) Data Analysis: Probit method for EiC50 (48 hr) and Binominal method for EiC50 (24 hr)
b) Method of Calculating Mean Measured Concentrations: Not applied

Result: [Measured Concentrations]
All of the measured concentrations were between 80 and 120% of the nominal concentrations (Table 1). Thus the nominal concentrations were used for calculating effect values.

Table 1.Measured concentrations of the test solutions in the 48-hour acute immobilisation test on Daphnia magna under the flow-through test conditions

Nominal concn. (mg/l)	Measured concn. (mg/l)		Arithmetic mean (mg/l)	Measured /Nominal (%)	
	0 h	48 h		0 h	48 h
Control	<0.005	<0.005	---	---	---
Solv. Control	<0.005	<0.005	---	---	---
0.10	0.111	0.112	0.112	111	112
0.18	0.214	0.198	0.206	119	110
0.32	0.359	0.284	0.322	112	89
0.56	0.622	0.544	0.583	111	97
1.0	1.10	1.01	1.06	110	101

[Water Chemistry]
Table 2.pH values of the test solutions in the 48-hour acute Immobilisation test on Daphnia magna under the flow-through test
conditions

Nominal concn. (mg/l)	pH	
	0 hour	48 hours
Control	7.8	7.7
Solvent control	7.8	7.7
0.10	7.8	7.7
0.18	7.8	7.7
0.32	7.8	7.7
0.56	7.8	7.7
1.0	7.8	7.6

Table 3.Dissolved oxygen concentrations (DO) of the test

solutions in the 48-hour acute immobilisation test on Daphnia magna under the flow-through test conditions

Nominal concn.	DO (mg/l)	
(mg/l)	0 hour	48 hours
Control	8.9	9.0
Solvent control	8.8	9.0
0.10	8.7	8.9
0.18	8.7	8.9
0.32	8.6	8.9
0.56	8.6	8.9
1.0	8.6	8.9

[Effect Data]
EiC50 (24 hr) : 0.72 mg/l (Table 4 & 5)
EiC50 (48 hr) : 0.38 mg/l
(95% confidence limits: 0.33 - 0.45mg/l)(Table 4 & 5)
EiC100 (48 hr) : 1.0 mg/l (Table 4 & 6)
NOECi (48 hr) : 0.10 mg/l (Table 4 & 6)

Table 4.Cumulative numbers of deaths or immobility on Daphnia magna

Nominal concn.	Cumulative number of deaths or immobility (Cumulative % of deaths or immobility)	
(mg/l)	24 hours	48hours
Control	0 (0)	0 (0)
Solvent. Control	0 (0)	0 (0)
0.10	0 (0)	0 (0)
0.18	0 (0)	1 (5)
0.32	0 (0)	4 (20)
0.56	1 (5)	18 (90)
1.0	2 (100)	20 (100)

Table 5.Calculated EiC50 values based on the nominal concentrations

Exposure Period (hours)	EiC50 (mg/l)	95% confidence limits (mg/l)	Statistical method
24	0.72	not calculated	Binominal
48	0.38	0.33 - 0.45	Probit

Table 6.No observed effective concentration (NOEC) and the lowest concentration in 100% mortality or immobility based on the nominal concentrations

Exposure Period (hours)	NOEC (mg/l)	Lowest concentration in 100% mortality or immobility (mg/l)

	24	0.32 1.0
	48	0.10 1.0

Reliability: (2) valid with restrictions
OECD TG study with use of solvent/dispersant
Flag: Critical study for SIDS endpoint
30-JUL-2004 (16)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Selenastrum capricornutum (Algae)
Endpoint: biomass
Exposure period: 72 hour(s)
Unit: mg/l Analytical monitoring: yes
NOEC: = .045 -
EC50: = .78 -

Method: OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year: 1999
GLP: yes
Test substance: other TS:Wako Pure Chemical Industries, Ltd., Purity 99.6 %, Lot No. PAM5243

Method: [Test Organisms]
a) Strain Number: ATCC22662
b) Supplier/Source: American Type Culture Collection
c) Pretreatment: Subcultured for 3 days in OECD medium before use.

[Test Conditions]
a) Medium: OECD medium (Table 1)
b) Exposure Vessel Type: 100-ml Medium in a 500-ml Conical Flask
c) Nominal Concentrations (as mg/l): 0, 0.10, 0.22, 0.46, 1.0, 2.2, 4.6 and 10
d) Dispersant and Concentrations: Polyoxyethylenesorbitan fatty acid ester, 10 mg/l test solution
e) Number of Replicates: 3
f) Initial Cell Number: 10,000 cells/ml
g) Water Temperature: 23+/-2 deg C
h) Light Condition: 4,000 - 5,000 lux, continuous

Table 1.The composition of OECD medium

Nutrient salt	Concentration (mg/l)
H3BO3	0.185
MnCl2.4H2O	0.415
ZnCl2	0.003
FeCl3.6H2O	0.08
Na3EDTA.2H2O	0.1
CoCl2.6H2O	0.0015
Na2MoO4.2H2O	0.007
CuCl2.2H2O	0.00001
CaCl2.2H2O	18
NH4Cl	15
KH2PO4	1.6
NaHCO3	50
MgCl2.6H2O	12

MgSO4.7H2O 15

[Analytical Procedure]
Portions of the test solutions were withdrawn at 0 hour and 72 hours and extracted with hexane. Concentrations of the test substance were determined by gas chromatography.

[Statistical Method]
a) Data Analysis: Doudoroff method for EbC50, simpre regression method for ErC50 and Dunnett's multicomparison method for NOEC
b) Method of Calculating Mean Measured Concentrations: Time-weighted mean concentrations

Result: [Measured Concentrations]
Measured concentrations at the beginning (0 hr) and the end (72 hr) of the test were ranged within 66 - 91% and 19 - 43% of the nominal concentrations, respectively. Because most of the measured concentrations were lower than 80% of the nominal, the time-weighted concentrations were used to calculate effect values (Table 2).

Table 2.Measured concentrations of the test solutions in the 72-hour growth inhibition test on Selenastrum capricornutum

Nominal concn. (mg/l)	Measured concn. (mg/l)		Time -weighted mean	Measured/Nominal (%)	
	0 hr	72 hr	(mg/l)	0 hr	72 hr
Control	<0.005	<0.005	---	---	---
Solv. Control	<0.005	<0.005	---	---	---
0.10	0.0833	0.0201	0.0445	83	20
0.22	0.185	0.0419	0.0964	84	19
0.46	0.303	0.0983	0.182	66	21
1.0	0.912	0.427	0.639	91	43
2.2	1.59	0.591	1.01	72	27
4.6	3.49	1.15	2.11	76	25
10	8.13	2.32	4.63	81	23

[Water Chemistry]
Table 3.The pH values of the test solutions in the 72-hour Growth inhibition test on Selenastrum capricornutum.

Nominal concn. (mg/l)	pH	
	0 hour	72 hours
Control	8.0	10.4
Solvent control	7.9	10.3
0.10	7.9	10.4
0.22	8.0	10.5
0.46	7.9	10.4
1.0	7.9	10.4
2.2	7.9	8.9
4.6	7.9	8.2
10	7.9	8.0

[Effect Data]
Area method:
EbC50 (0 - 72 hr) = 0.78mg/l (Table 4 - 6)
NOEC (0 - 72 hr) = 0.045 mg/l (Table4, 5 & 7)
Rate method:
ErC50 (0 - 24 hr) = 1.5 mg/l
(95% confidence limits: 1.2 - 1.9 mg/l) (Table 4 - 6)
NOEC (0 - 24 hr) = 0.096 mg/l (Table4, 5 & 7)
ErC50 (24 - 48 hr) = 1.2 mg/l
(95% confidence limits: 1.16 - 1.21 mg/l) (Table 4 - 6)
NOEC (24 - 48 hr) = 0.64 mg/l (Table4, 5 & 7)
ErC50 (24-72hr) = 1.2 mg/l
(95% confidence limits: 1.1 - 1.3 mg/l) (Table 4 - 6)
NOEC (24 - 72 hr) = 0.18 mg/l (Table4, 5 & 7)

Table 4.Mean cell concentrations and their standard deviations (S. D.) in the test cultures and controls

Nominal concn (mg/l)	Cell concentration (x 10000 cells/ml)	0 hr	24 hr	48 hr	72 hr
Control	Mean	1.0	6.98	34.51	89.12
	S. D.	0.0	0.28	1.37	0.65
Solvent control	Mean	1.0	7.19	37.96	90.52
	S. D.	0.0	0.23	2.91	3.79
0.10	Mean	1.0	6.82	35.32	85.47
	S. D.	0.0	0.45	1.07	4.37
0.22	Mean	1.0	6.49	33.39	76.51
	S. D.	0.0	0.37	3.08	6.09
0.46	Mean	1.0	5.70	30.85	65.81
	S. D.	0.0	0.24	0.98	0.91
1.0	Mean	1.0	5.58	28.18	61.64
	S. D.	0.0	0.37	2.38	4.74
2.2	Mean	1.0	2.73	7.23	17.51
	S. D.	0.0	0.11	0.30	1.01
4.6	Mean	1.0	1.90	2.00	2.17
	S. D.	0.0	0.06	0.06	0.10
10	Mean	1.0	1.55	1.59	1.58
	S. D.	0.0	0.05	0.03	0.08

Table 5.Percent inhibition of the cell growth (IA) and the average specific growth rates (Im) in the 72-hour growth inhibition test on Selenastrum capricornutum

Nominal concn.	Area A	Inhibition IA (%)	Rate M	Inhibition Im (%)
(mg/l)	(0-72 hr)		0-24 hr)	

Control	20050800	---	0.080918	---
Solv. cont.	21099600	-5.23	0.082181	-1.56
0.10	19769600	1.40	0.079954	1.19
0.22	18151600	9.47	0.077859	3.78
0.46	16068400	19.86	0.072471	10.44
1.0	14899600	25.69	0.071574	11.55
2.2	3891600	80.59	0.041823	48.31
4.6	596400	97.03	0.026732	66.96
10	343600	98.29	0.018244	77.45

Table 5.continue

Nominal concn.	Rate M	Inhibition Im (%)	Rate M	Inhibition Im (%)
(mg/l)	(24-48 hr)		(24-72 hr)	
Control	0.066612	---	0.053081	---
Solv. cont.	0.069260	-3.98	0.052764	0.60
0.10	0.068548	-2.91	0.052675	0.77
0.22	0.068197	-2.38	0.051387	3.19
0.46	0.070396	-5.68	0.050988	3.94
1.0	0.067441	-1.24	0.050032	5.75
2.2	0.040579	39.08	0.038706	27.08
4.6	0.002138	96.79	0.002760	94.80
10	0.001073	98.39	0.000436	99.18

Table 6.Calculated EC50 values

	Value (mg/l)	95% confidence limits (mg/l)	Ordinate
EbC50 (0-72 hr)	0.78	not calculated	IA
ErC (0-24 hr)	1.5	1.2 - 1.9	Im
ErC (24-48 hr)	1.2	1.16 - 1.21	Im
ErC (24-72 hr)	1.2	1.1 - 1.3	Im

Table 7.Calculated NOEC

	Value (mg/l)	Statistical method	Parameter
NOEC (0-72 hr)	0.045	Dunnett (p<0.05)	IA
NOEC (0-24 hr)	0.096	Dunnett (p<0.05)	Im
NOEC (24-48 hr)	0.64	Dunnett (p<0.05)	Im
NOEC (24-72 hr)	0.18	Dunnett (p<0.05)	Im

Reliability: (2) valid with restrictions
OECD TG study with use of dispersant
Flag: Critical study for SIDS endpoint
30-JUL-2004 (15) (24)

4.4 Toxicity to Microorganisms e.g. Bacteria
-

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish
-

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Endpoint: reproduction rate
Exposure period: 21 day(s)
Unit: mg/l Analytical monitoring: yes
NOEC: = .02 -
EC50: = .23 -
LC50 : = .39 -

Year: 1999
GLP: yes
Test substance: other TS:Wako Pure Chemical Industries, Ltd., Purity 99.6 %, Lot No. PAM5243

Method: OECD Guideline 211

[Test Organisms]
a) Age: < 24 hours old
b) Supplier / Source: National Institute for Environmental Studies (JAPAN)

[Test Conditions]
a) Dilution Water Source: Laboratory supply water (dechlorinated)
b) Dilution Water Chemistry:
Hardness: 87 - 88 mg/l (as CaCO3)
PH : 7.6 - 8.2

Table 1.Water quality of dilution water

Parameter	Concentration
Coliform group	ND
Cadmium	< 0.001 mg/l
Mercury	< 0.0001 mg/l
Selenium	< 0.001 mg/l
Lead	< 0.005 mg/l
Arsenic	< 0.001 mg/l
Chromium (VI)	< 0.005 mg/l
Cyanide	< 0.005 mg/l
Nitrate and nitrite	0.2 mg/l
Fluoride	0.20 mg/l
Carbon tetrachloride	< 0.0002 mg/l
1,2-Dichloroethane	< 0.0002 mg/l
1,1-Dichloroethylene	< 0.001 mg/l
Dichloromethane	0.002 mg/l
Cis-1,2-Dichloroethylene	< 0.001 mg/l
Tetrachloroethylene	< 0.001 mg/l
1,1,2-Trichloroethane	< 0.0005 mg/l
Trichloroethylene	< 0.001 mg/l
Benzene	< 0.001 mg/l
Chloroform	< 0.001 mg/l

Dibromochloromethane	< 0.001 mg/l
Bromochloromethane	< 0.001 mg/l
Bromoform	< 0.001 mg/l
Trihalomethanes	< 0.001 mg/l
1,3-Dichloropropene	< 0.0002 mg/l
Simazine	< 0.0002 mg/l
Thiram	< 0.0005 mg/l
Thiobencarb	< 0.001 mg/l
Zinc	< 0.005 mg/l
Iron	< 0.03 mg/l
Copper	< 0.01 mg/l
Sodium	30 mg/l
Manganese	< 0.005 mg/l
Chloride	49 mg/l
Total hardness (as CaCO3)	87 mg/l
Total residue	180 mg/l
Surface active agents (anionic)	< 0.02 mg/l
1,1,1-Trichloroethane	< 0.001 mg/l
Phenols	< 0.005 mg/l
Permanganate reduction substances	1.1 mg/l
PH Value	7.9
Taste	Normal
Odor	Normal
Color	< 1 degree
Turbidity	< 1 degree
Phosphorus	< 0.01 mg/l
Alminium	< 0.05 mg/l
Nickel	< 0.001 mg/l
Tin	< 0.1 mg/l
Free residual chlorine	< 0.01 mg/l
Bromide	< 0.5 mg/l
Sulfide	< 0.01 mg/l
Ammonium	< 0.05 mg/l
Electric conductivity	350 uS/cm
Alkalinity (as CaCO3)	46 mg/l
Potassium	7.1 mg/l
Calcium	20 mg/l
Magnesium	8.7 mg/l
PCB	< 0.0005 mg/l
Organophosphate	< 0.02 mg/l

c) Exposure Vessel Type: 80-ml test solution in a 100-ml glass bottle
d) Nominal Concentrations (as mg/l):
Test 1; 0, 0.0022, 0.0046, 0.010, 0.022, 0.046, 0.10 and 0.22
Test 2; 0, 0.10, 0.22. 0.46 and 1.0
*In the test1, the maximum concentration (0.22 mg/l) caused a only 24.7 % reduction in reproduction rate. Therefore, the test 2 was conducted at more higher concentration.
e)Dispersant and Concentrations: Polyoxyethylenesorbitan fatty acid ester, 0.22 mg/l (Test 1) and 1.0 mg/l (Test 2)
f) Number of Replicates: 10
g) Individuals per Replicates: 1
h) Renewal Rate of Test Water: Total solution in a vessel was renewed every 48 hours (2 days).
I) Water Temperature: 19.2 - 20.7 deg C
J) Light Condition: 16:8 hours, light-darkness cycle, not brighter than 1,200 lux

k) Feeding: Fed on Chlorella vulgaris at 0.15 mg carbon/day/individual.

[Analytical Procedure]
Portions of the test solutions were withdrawn at 0 hour, on the 2nd day before renewal, on the 6th day after renewal, on the 8th day before renewal, on the 14th day after renewal and on the 16th day before renewal. The withdrawn samples were extracted with hexane and concentrations of the test substance were determined by gas chromatography.

[Statistical Method]
a) Data Analysis: Binominal method for LC50, single regression method for EC50, and Dunnett's multicomparison method for NOEC and LOEC.
b) Method of Calculating Mean Measured Concentrations: Time-weighted mean concentrations

Result: [Measured Concentrations]
Measured concentrations of the test solutions just after renewal (fresh preparation) and those 48 hour after renewal were ranged within 81 - 117% and 10 - 27% of the nominal concentrations, respectively. Because all of the measured concentrations at 48 hour after renewal were lower than 80% of the nominal, the time-weighted concentrations were used to calculate the effect values (Table 2 & 3).

Table 2.Measured concentrations of the test solutions in the 21-day reproduction test on Daphnia magna under the semi-static test conditions

Nominal concn. (mg/l)	Measured Concn. (mg/l)		Time-weighted mean (mg/l)	Measured/Nominal (%)	
	Day 0 fresh	Day 2 old		Day 0 fresh	Day 2 old
(Test 1)					
Control	<0.0001	<0.0001	---	---	---
Solv. cont.	<0.0001	<0.0001	---	---	---
0.0022	0.00233	0.000212	0.000884	106	10
0.0046	0.00496	0.000559	0.00202	108	12
0.010	0.0107	0.00146	0.00464	107	15
0.022	0.0210	0.00324	0.00950	95	15
0.046	0.0528	0.00558	0.0210	115	12
0.10	0.0865	0.0143	0.0401	87	14
0.22	0.184	0.0326	0.0875	84	15
(Test 2)					
Control	<0.0001	<0.0001	---	---	---
Solv. cont.	<0.0001	<0.0001	---	---	---
0.10	0.102	0.0187	0.0491	102	19
0.22	0.228	0.0466	0.114	104	21
0.46	0.484	0.113	0.255	105	25
1.0	1.16	0.226	0.571	116	23

Table 2 - continued (1).

Nominal	Measured	Time	Measured/Nominal

Nominal concn. (mg/l)	Measured Concn. (mg/l)		Time-weighted mean (mg/l)	Measured/Nominal (%)	
	Day 6 fresh	Day 8 old		Day 6 fresh	Day 8 old
(Test 1)					
Control	<0.0001	<0.0001	---	---	---
Solv. cont.	<0.0001	<0.0001	---	---	---
0.0022	0.00241	<0.0001	0.000499	110	---
0.0046	0.00411	0.000663	0.00189	89	14
0.010	0.0109	0.000966	0.00410	109	10
0.022	0.0216	0.00311	0.00954	98	14
0.046	0.0373	0.00678	0.0179	81	15
0.10	0.0952	0.0144	0.0428	95	14
0.22	0.222	0.0334	0.0996	101	15
(Test 2)					
Control	<0.0001	<0.0001	---	---	---
Solv. cont.	<0.0001	<0.0001	---	---	---
0.10	0.0959	0.0220	0.0502	96	22
0.22	0.219	0.0526	0.117	100	24
0.46	0.540	0.126	0.284	117	27

Table 2 - continued (2).

Nominal concn. (mg/l)	Measured Concn. (mg/l)		Time-weighted mean (mg/l)	Measured/Nominal (%)	
	Day 14 fresh	Day 16 old		Day 14 fresh	Day 16 old
(Test 1)					
Control	<0.0001	<0.0001	---	---	---
Solv. cont.	<0.0001	<0.0001	---	---	---
0.0022	0.00213	0.000245	0.000872	97	11
0.0046	0.00448	0.000603	0.00193	97	13
0.010	0.00873	0.00166	0.00426	87	17
0.022	0.0237	0.00381	0.0109	108	17
0.046	0.0420	0.00754	0.0201	91	16
0.10	0.0916	0.0140	0.0413	92	14
0.22	0.240	0.0388	0.110	109	18
(Test 2)					
Control	<0.0001	<0.0001	---	---	---
Solv. cont.	<0.0001	<0.0001	---	---	---
0.10	0.0988	0.0210	0.0502	99	21
0.22	0.218	0.0533	0.117	99	24
0.46	0.512	0.126	0.275	111	27

Table 3.The time-weighted mean values for the measured concentrations of test solutions in periods during the 21-day reproduction test on Daphnia magna under the semi-static test conditions

Nominal concn.	Time-weighted mean value (mg/l)	Mean Value/Nominal (%)

(mg/l)

	0-7d.	0-14d.	0-21d.	0-7d.	0-14d.	0-21d.
(Test 1)						
0.0022	0.000884	0.000691	0.000751	40	31	34
0.0046	0.00202	0.00195	0.00195	44	42	42
0.010	0.00464	0.00437	0.00433	46	44	43
0.022	0.00950	0.00952	0.00997	43	43	45
0.046	0.0210	0.0195	0.0197	46	42	43
0.10	0.0401	0.0414	0.0414	40	41	41
0.22	0.0875	0.0935	0.0992	40	43	45
(Test 2)						
0.10	0.0491	0.0496	0.0498	49	50	50
0.22	0.114	0.115	0.116	52	52	53
0.46	0.255	0.270	0.272	55	59	59
1.0	0.571	---a	---a	57	---a	---a

d.: days
a:All of the parental animals died before Day 21 and thus the time-weighted mean value was not calculated for the period.

[Water Chemistry]
pH: 7.8 - 8.7 (Test 1), 7.8 - 8.8 (Test 2)
Dissolved oxygen (mg/l): 8.4 - 9.8 (Test 1),
8.6- 9.7 (Test 2)
Total hardness (mg/l as CaCO3): 87 - 88 (Test 1),
85 - 88 (Test 2)

[Effect Data (reproduction)]
All of the following effect values were calculated with the measured concentrations. NOEC and LOEC values were determined on the basis of reproduction using the data of Test 1.

LC50 (21 days) = 0.39 mg/l (parental mortality)
(Table 4 & 5)
EC50 (21 days) = 0.23 mg/l
(95% Confidence limits: 0.22 - 0.24 mg/l)
(Table 7 - 9)
NOEC (21 days) = 0.020 mg/l (Table 7 & 8)
LOEC (21 days) = 0.041 mg/l (Table 7 & 8)

Table 4.Cumulative numbers of deaths among the parental animal groups

Nominal concn. (mg/l)	Cumulative number of deaths on Day: 0	1	2	3	4	5	6	7	8	9	10
(Test 1)											
Control	0	0	0	0	0	0	0	0	0	0	0
Solv. cont.	0	0	0	0	0	0	0	0	0	0	0
0.0022	0	0	0	0	0	0	0	0	0	0	0
0.0046	0	0	0	0	0	0	0	0	0	0	0
0.010	0	0	0	0	0	0	0	0	0	0	0
0.022	0	0	0	0	0	0	0	0	0	0	0
0.046	0	0	0	0	0	0	0	0	0	0	0
0.10	0	0	0	0	0	0	0	0	0	0	0
0.22	0	0	0	0	0	0	0	0	0	0	0

(Test 2)											
Control	0	0	0	0	0	0	0	0	0	0	0
Solv. cont.	0	0	0	0	0	0	0	0	0	0	0
0.10	0	0	0	0	0	0	0	0	0	0	0
0.22	0	0	0	0	0	0	0	0	0	0	0
0.46	0	0	0	0	0	0	0	0	0	0	0
1.0	0	0	0	3	10	10	10	10	10	10	10

Table 4 - continued.

Nominal concn. (mg/l)	Cumulative number of deaths on Day: 11	12	13	14	15	16	17	18	19	20	21
(Test 1)											
Control	0	0	0	0	0	0	0	0	0	0	0
Solv. cont.	0	0	0	0	0	0	0	0	0	0	0
0.0022	0	0	0	0	0	0	0	0	0	0	0
0.0046	0	0	0	0	0	0	0	0	0	0	0
0.010	0	0	0	0	0	0	0	0	0	0	0
0.022	0	0	0	0	0	0	0	0	0	0	0
0.046	0	0	0	0	0	0	0	0	0	0	0
0.10	0	0	0	0	0	0	0	0	0	0	0
0.22	0	0	0	0	0	0	0	0	0	0	0
(Test 2)											
Control	0	0	0	0	0	0	0	0	0	0	0
Solv. cont.	0	0	0	0	0	0	0	0	0	0	0
0.10	0	0	0	0	0	0	0	0	0	0	0
0.22	0	0	0	0	0	0	0	0	0	0	0
0.46	0	0	0	0	0	0	0	0	0	0	0
1.0	10	10	10	10	10	10	10	10	10	10	10

Table 5.Cumulative mortality of parental animal groups (%)

Nominal concn. (mg/l)	Cumulative percentage of deaths on Day: 1	2	4	7	14	21
(Test 1)	0	0	0	0	0	0
Control	0	0	0	0	0	0
Solv. cont.	0	0	0	0	0	0
0.0022	0	0	0	0	0	0
0.0046	0	0	0	0	0	0
0.010	0	0	0	0	0	0
0.022	0	0	0	0	0	0
0.046	0	0	0	0	0	0
0.10	0	0	0	0	0	0
0.22	0	0	0	0	0	0
(Test 2)						
Control	0	0	0	0	0	0
Solv. cont.	0	0	0	0	0	0
0.10	0	0	0	0	0	0
0.22	0	0	0	0	0	0
0.46	0	0	0	0	0	0
1.0	0	0	100	100	100	100

Table 6.The time of the first production of juveniles (days)

Nominal concn. (mg/l)	Bottle number 1	2	3	4	5	6	7	8	9	10	Mean
(Test 1)											
Control	8	8	8	9	8	8	8	8	8	8	8.1
Solv. cont.	8	8	8	8	8	8	8	8	9	9	8.2
0.0022	8	8	8	8	8	8	9	8	8	9	8.2
0.0046	9	8	8	8	8	9	8	8	8	9	8.3
0.010	8	8	9	8	9	9	8	8	8	8	8.3
0.022	8	8	8	9	8	8	8	9	9	8	8.3
0.046	8	8	8	8	9	8	9	8	8	8	8.2
0.10	8	8	8	8	8	8	8	8	9	8	8.1
0.22	8	8	9	8	8	8	8	8	8	8	8.1
(Test 2)											
Control	8	8	8	8	8	8	8	8	8	9	8.1
Solv. cont.	8	8	8	8	9	8	8	8	9	8	8.2
0.10	8	8	8	8	8	8	8	8	8	8	8.0
0.22	10	10	8	8	9	8	9	8	8	10	8.1
0.46	15	11	13	12	11	10	13	11	12	13	12.1
1.0	D	D	D	D	D	D	D	D	D	D	---a

D: The parental animal died before producing juveniles.
a:No production of juveniles during the 21-day test period.

Table 7.Mean cumulative numbers of juveniles produced per parental animal survived for 21 days

Nominal concn. (mg/l)	Mean cumulative number on Day: 0	7	8	9	10	11	12	13
(Test 1)								
Control	0.0	0.0	4.2	4.9	4.9	25.5	29.0	29.0
Solv. cont.	0.0	0.0	3.2	3.8	3.8	21.0	25.2	25.2
0.0022	0.0	0.0	5.1	6.7	6.7	23.6	28.2	28.2
0.0046	0.0	0.0	4.8	6.4	6.4	22.2	28.2	28.2
0.010	0.0	0.0	4.6	6.2	6.2	24.4	31.1	31.1
0.022	0.0	0.0	3.8	5.6	5.6	20.9	28.0	28.0
0.046	0.0	0.0	5.1	5.9	5.9	22.6	27.5	27.5
0.10	0.0	0.0	0.2	0.2	0.2	12.2	13.4	13.4
0.22	0.0	0.0	0.0	0.0	0.0	8.3	9.0	9.0
(Test 2)								
Control	0.0	0.0	9.0	10.5	10.5	29.0	35.4	35.4
Solv. cont.	0.0	0.0	5.9	8.1	8.1	24.7	31.5	31.5
0.10	0.0	0.0	10.4	10.4	10.4	31.5	31.5	31.5
0.22	0.0	0.0	3.3	5.4	9.0	19.0	24.0	33.8
0.46	0.0	0.0	0.0	0.0	0.8	3.3	5.0	7.1
1.0	0.0	---a	---a	---a	---a	---a	---a	---a

Table 7 - continued.

Nominal concn. (mg/l)	Mean cumulative number on Day: 14	15	16	17	18	19	20	21
(Test 1)								
Control	53.3	56.8	56.8	84.6	88.0	88.0	96.6	115.5
Solv. cont.	49.9	55.7	55.7	81.2	87.4	87.4	95.6	115.0
0.0022	53.9	60.4	60.4	82.4	87.0	87.0	103.4	110.0
0.0046	50.7	61.0	61.0	78.9	88.7	88.7	105.7	116.9
0.010	56.3	67.6	67.6	88.3	97.5	97.5	112.1	121.7
0.022	51.0	59.7	59.7	79.9	87.5	87.5	102.9	112.8
0.046	52.0	58.2	58.2	80.6	86.0	86.0	106.9	112.4
0.10	39.3	41.1	41.1	64.5	67.1	67.1	91.6	94.6
0.22	32.8	35.2	35.2	56.9	59.4	59.4	84.1	87.0
(Test 2)								
Control	57.8	63.3	63.3	86.0	91.6	91.6	108.4	115.2
Solv. cont.	53.6	63.5	63.5	86.3	93.7	93.7	102.0	122.6
0.10	62.6	62.6	62.6	87.3	87.3	87.3	111.5	114.0
0.22	47.2	51.4	57.6	72.7	78.6	88.7	101.1	101.1
0.46	12.3	16.3	21.2	28.9	34.8	37.0	40.7	45.3
1.0	---a	---a	---a	---a	---a	---a	---a	---a

a:Not counted because the parental animal died before producing juveniles.

Table 8.Cumulative numbers of juveniles per parental animal survived for 21 days in Test 1.

Bottle No.	Nominal concn., mg/l (Measured concn., mg/l) Control	Solv. cont.	0.0022 (0.000751)	0.0046 (0.00195)	0.010 (0.00433)
1	126	105	103	124	109
2	113	112	111	110	122
3	115	112	112	111	102
4	113	116	110	119	100
5	113	131	108	115	114
6	122	114	115	126	146
7	108	124	109	116	143
8	116	106	118	107	122
9	121	116	106	123	109
10	108	114	108	118	131
Mean	115.5	115.0	110.0	116.9	121.7
S.D.	5.9	7.7	4.3	6.3	14.6
Inhibition rate(%)	---	0.4	4.8	-1.2	-5.4

Significant difference	---	NS	NS	NS	NS

Table 8 - continued.

Bottle No.	Nominal concn., mg/l (Measured concn.,mg/l)			
	0.022 (0.00997)	0.046 (0.0197)	0.10 (0.0414)	0.22 (0.0992)
1	103	118	84	94
2	119	105	84	82
3	99	115	106	85
4	100	109	103	86
5	118	113	96	85
6	124	107	93	96
7	114	115	107	86
8	110	110	87	86
9	111	115	86	85
10	130	117	100	85
Mean	112.8	112.4	94.6	87.0
S.D.	10.3	4.4	9.1	4.4
Inhibition rate (%)	2.3	2.7	18.1	24.7
Significant difference(a)	NS	NS	##	##

(a)Indicates a significant difference from the control determined by the Dunnett's multicomparisons procedure, one-sided test.

NS : not significant (p >= 0.05)
\# : significant (p < 0.05)
: significant (p < 0.01)

Table 9.Cumulative numbers of juveniles per parental animal survived for 21 days in Test 2.

Bottle No.	Nominal concn., mg/l (Measured concn.,mg/l)					
	Cont.	S. C.	0.10 (0.0498)	0.22 (0.116)	0.46 (0.272)	1.0 (0.571)
1	104	116	114	107	34	D
2	109	123	115	106	43	D
3	129	123	104	108	45	D
4	110	118	114	121	53	D
5	117	115	111	77	50	D
6	108	110	123	94	41	D
7	117	129	132	95	39	D
8	120	128	117	119	74	D
9	111	123	100	100	42	D

	10	127	141	110	84	32	D
Mean		115.5	122.6	114.0	101.1	45.3	---
S.D.		8.3	8.8	9.0	14.1	11.9	---
Inhibition rate (%)	---		-6.4	1.0	12.2	60.7	---
Significant difference(a)	---		NS	NS	##	##	---

D: Not calculated because the parental animal was dead before producing juveniles.
(a)Indicates the significant difference from the control by Dunnett's multicomparison procedure, one-sided test.
NS : not significant (p >= 0.05)
: significant (p < 0.05)
: significant (p < 0.01)

Reliability: (2) valid with restrictions
OECD TG study with use of dispersant
Flag: Critical study for SIDS endpoint
25-NOV-2004 (17)

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Sediment Dwelling Organisms
-

4.6.2 Toxicity to Terrestrial Plants
-

4.6.3 Toxicity to Soil Dwelling Organisms
-

4.6.4 Toxicity to other Non-Mamm. Terrestrial Species
-

4.7 Biological Effects Monitoring
-

4.8 Biotransformation and Kinetics
-

4.9 Additional Remarks

Remark: OCBC is hydrolyzed to o-chlorobenzyl alcohol with half-life of 33hr at pH7 under 25 deg C. Although no toxicity data is available for this substance, the toxicity values of o-chlorobenzyl alcohol is estimated by ECOSAR (ECOWIN v0.99g).

ECOSAR	Organism	Duration	End point	Estimated

Class				mg/l (ppm)
Benzyl Alcohols	Fish [CLOGP]	96-hr	LC50	189.7
Benzyl Alcohols	Fish [SRC]	96-hr	LC50	15.7
Benzyl Alcohols	Daphnid [CLOGP]	48-hr	LC50	0.6
Benzyl Alcohols	Daphnid [SRC]	48-hr	LC50	0.3

24-NOV-2004 (5)

5.0 Toxicokinetics, Metabolism and Distribution
-

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Strain: Sprague-Dawley
Sex: male/female
No. of Animals: 60
Vehicle: other: 0.1% Tween80
Value: = 783 - 951 mg/kg bw

Method: OECD Guide-line 401 "Acute Oral Toxicity"
Year: 1999
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: LD50
male: 951 mg/kg bw (715-1435 mg/kg bw)
female: 783 mg/kg bw (611-1011 mg/kg bw)
Result: All animals at 1400 mg/kg, two males and four femals at 1000 mg/kg, two femals at 700 mg/kg, and one male at 500 mg/kg died until 2days afer treatment. Salivation, lacrimation, flushing, decrease in locomotor activity, loose stool, abnormal gait were observed in surviving animals, and adoption of prone position, irregular respiration, hypothermia and ptosis were also observed on animals that died. The gross necropsy findings for the animals found dead included erosion/ulcer of glandular stomach, and histopathological changes were submucosa edema of forestomach and ulceration of glandular stomach. At the
terminal necropsy, thickening of the forestomach wall, erosion/ulcer of forestomach and adhesion of the organs in abdominal cavity were observed. The histopathological examination of surviving animals revealed ulceration, squamous epithelium hyperplasia, inflammatory cellular infiltration and granulation tissue in the forestomach, and peritonitis in the serous membrane.

Table 1. Mortality of rats treated orally with o-chlorobenzyl chloride (OCBC)

Sex	Dose (mg/kg)	Number of animals	Number of deaths (Days: 1	2	3	4-15)	Mortality
Male	0	5	0	0	0	0	0/5
	350	5	0	0	0	0	0/5
	500	5	0	1	0	0	1/5
	700	5	0	0	0	0	0/5
	1000	5	1	1	0	0	2/5
	1400	5	5	0	0	0	5/5
Female	0	5	0	0	0	0	0/5

350	5	0	0	0	0	0/5
500	5	0	0	0	0	0/5
700	5	2	0	0	0	2/5
1000	5	3	1	0	0	4/5
1400	5	5	0	0	0	5/5

Test condition: The test material was administered by oral gavage. Each five rats for both sexs were used for the doses of 350, 500, 700, 1000 and 1400 mg/kg. Animals were fasted overnight (for approximately 18 hours) prior to administration. During the experiments the animals were allowed to access to food and water ad libitum. They were weighed individually before treatment and at 4, 8 and 15 days after treatment. The animals were observed five times on the day of treatment and daily thereafter for 14 days. Any symptoms of toxic signs of the animals were recorded. Necropsy was made on all dead animals. The surviving animals were sacrificed and necropsied.
Test substance: -Source: Ihara Chemical Industry Co., Ltd.-Lot No.T7030-Purity: 99.65%
Reliability: (1) valid without restriction
OECD Guideline study
Flag: Critical study for SIDS endpoint
24-NOV-2004 (31)

Type: LD50
Species: rat
Strain: Sprague-Dawley
Sex: male/female
No. of Animals: 40
Vehicle: no data
Value: = 350 - 880 mg/kg bw

Method: other:FIFRA Pesticide Assessment Guidelines, Subdivision F, Section 81-1, "Acute Oral Toxicity Study" TSCA Health effects Test Substances, " Acute exposure, Oral Toxicity"
Year: 1986
GLP: yes
Test substance: other TS:- Source: Monsanto Company- Lot/Batch No.: 3168723, 2503577

Remark: LD50
Male: 880 mg/kg bw (95% confidence limits 512-1248 mg/kg bw),
Female: 350 mg/kg bw (95% confidence limits was not determined)
Male and female: 570 mg/kg (95% confidence limits 380-760 mg/kg)
The method was in principle equivalent to OECD Guideline 401.
Result: All male and female rats at 2000 mg/kg, four males and all females at 1000 mg/kg, all females at 500 mg/kg died at the first or the second day. Other rats survived for 14 days. Signs seen on the day of dosing in all groups included oral, nasal and ocular discharge, hypoactivity, soft stool and fecal and urinary staining. Antemortem signs in animals which died also included ataxia, prostration, wet rales, hypopnea and hypothermia. All surviving animals had

decreased food consumption on the day after dosing and several had unthrifty coats, this continued in some animals through Day 7. However, most surviving animals were free of abnormalities from Day 8 through termination of the study (Day 14). Necropsy of animals which were found dead revealed a variety of changes, primarily in the lungs and gastrointestinal tract. Some dead animals exhibited changes in the stomach and intestine which were suggestive of an irritant effect (the presence of red fluid material, discoloration or thickening of walls). No substance-related abnormalities were found in any survived animals. Oral LD50 with 95% confidence limits was calculated to be 880 (512-1248) mg/kg for male, 350 mg/kg for female (confidence limits cannot be calculated due to distribution of mortality) , and 570 (380-760) mg/kg for combined both sexes.

Table 1.Summary of the observed signs in the acute oral toxicity study with OCBC.

Dose levels (mg/kg)	Mortality Male	Female	Signs
250	0/5	0/5	The following signs were observed: nasal discharge, oral discharge, ocular discharge, urinary staining, fecal staining, unthrifty coat, soft stool, hypoactivity and food consumption decrease
500	0/5	5/5	All females died through 6 hours after dosing. The following signs were observed: ataxia, nasal, oral and ocular discharge, hypopnea, urinary staining, fecal staining, unthrifty coat, soft stool, hypoactivity, prostration and food consumption decrease
1000	4/5	5/5	All females died through 6 hours after dosing. Four males died through 2 days after dosing. The following signs were observed: ataxia, nasal, oral and ocular discharge, hypopnea, wet rales, urinary staining, fecal staining, unthrifty coat, soft stool, hypothermia, hypoactivity, prostration and food consumption decrease
2000	5/5	5/5	All rats died through 23 hours after dosing. The following signs were observed: ataxia, nasal, oral and ocular discharge, hypopnea, wet

	rales, urinary staining, fecal staining, soft stool, hypoactivity, and prostration

Test condition: Five males and five females were used for each dose group. Animals were individually housed in suspended stainless steel cages with wire mesh bottoms under 12-h light and 12-h dark cycle condition. Room temperature and humidity were maintained within the range of 67-76F and 30-70%. Commercial laboratory feed and water were freely given except for approximately 18 hours prior to the treatment. Test substance was administrated by oral intubation, using a ball-tipped intubation needle fitted onto a syringe at dose levels of 250, 500, 1000, and 2000 mg/kg. Following administration, obsevations were made three times at the first day and once daily thereafter for 14 days. Animals were weighed just prior to dosing, on Day 7 and Day 14. Any symptoms of toxicity of the animals were recorded. Necropsy was made on all dead animals. The surviving animals were sacrificed and necropsied. LD50 with 95% confidence limits was calculated according to the method of L. C. Miller and M. L. Tainter, Proc. Soc. Exp. Bio. Med. 57: 261-264 (1944).

Reliability: (1) valid without restriction
Test procedure according to national standards (EPA)

24-NOV-2004 (32)

Type: LD50
Species: rat
Strain: Sprague-Dawley
Sex: male/female
No. of Animals: 30
Vehicle: other:0.5% w/v methylcellulose
Value: = 533 - 690 mg/kg bw

Method: other:EPA guidelines for registering Industrial Chemicals in the U.S., Pesticide Assessment Guidelines, Subdivision F, Section 81-1, TSCA Health effects Test Guidelines, 40 CFR798.1175
Year: 1993
GLP: yes
Test substance: other TS:- Source: Miki and Co., LTD- Lot No.: V1007- Purity : 99.64%

Remark: LD50
Male: 690 mg/kg bw (95% confidence limits 507-939 mg/kg bw),
Female: 533 mg/kg bw (95% confidence limits 306-928 mg/kg bw)
Combined: 618 mg/kg bw (95% confidence limits 475-805 mg/kg bw)

The method was in principle equivalent to OECD Guideline 40
Result: All deaths occured within one day of dosing. There were 3/10, 7/10 and 8/10 deaths in the 500, 720, and 1037 mg/kg dose groups, respectively. Clinical signs of systemic toxicity were noted in all dose groups. The majority of rats had urogenital staining, evidence of salivation, reddened extremities (nose, ears, forepaws and/or forelimbs), hypoactivity, abnormal defecation (mucoid feces, soft stool), ocular discharge and dried red stainig around the mouth on the day of dosing. In general, clinical sighs of systemic toxicity

subsided by day 2 and all surviving animals appeared normal by day 6 or earlier. Other findings included ataxia, hypothermia, bradypnea and prostration for rats that died during the study. The majority of surviving females suffered reduced weight gains during the study.
Kidney abnormalities (reddend appearance, reddened cortico-medullary injuction, dilated pelvis) were noted for all animals that died during the study. Other gross necropsy findings for the animals that died included dark red adrenal glands, hemmorrhagic thymus glands and gastric abnormalities. At the terminal necropsy, gastric abnormalities (primarily thickened mucosa and adhesions) were observed for all surviving females and one male in 1037 mg/kg dose group. There were no other gross necropsy findings for animals survived.

Table 1.Mortality of treated orally with OCBC.

	Number of deaths					
Dose	Days					
(mg/kg)	0	1	2	3	4-14	Total
	M/F	M/F	M/F	M/F	M/F	M/F
500	0/2	1/0	0/0	0/0	0/0	1/2
720	0/4	3/0	0/0	0/0	0/0	3/4
1037	2/3	2/1	0/0	0/0	0/0	4/4

Test condition: Animals were individually housed in suspended wire-mesh cages under 12-h light and12-h dark cycle condition. Room temperature and humidity were maintained within the range of 70-75F and 28-60%. The room humidity was slightly below the guidelines specified range on one day. A brief period of decreased humidity would not be expected to adversely affect the health of the animals. Therefore, this deviation has no impact on the scientific validity, integrity or objective of this study. Commercial laboratory feed and water were freely available except for approximately 18-20 hours prior to the treatment. Three groups of five male and five female rats were administered orally with single doses at levels of 500, 720 and 1037 mg/kg, using gastric intubation with ball-tipped oral dosing needles which affixed to the appropriate size syringes. The rats were returned to feed 3-4 hours after dosing, and observed at approximately 1, 3 and 4 hours post-dose on day 0 and daily thereafter for 14 days. Animals were weighed just prior to dosing, on day 7, 14 and at necropsy. Necropsy was made on all dead animals. The surviving animals were weighed, sacrificed and necropsied.
Reliability: (1) valid without restriction
Test procedure according to national standards (EPA)
25-NOV-2004 (22)

Type: LD50
Species: rat
Strain: Sprague-Dawley
Sex: male/female
No. of Animals: 40

Vehicle: no data
Value: = 430

Method: other
Year: 1984
GLP: yes
Test substance: other TS:- Source: Occidental Chemical Corporation

Remark: LD50
430 mg/kg bw (95% confidence limits: 380-490 mg/kg bw)
The method was in principle equivalent to OECD Guideline 401.
Result: All male and female rats at 540 and 760 mg/kg, and three female at 390 mg/kg died at the first day. Other rats were survived for 14 days. Decreased motor activity and respiration, diarrhea, salivation and chromodacryorrhea were observed. There were no gross tissue changes observable at the necropsy. The oral LD50 with 95% confidence limits was calculated to be 430 (380 - 490) mg/kg.

Table 1.Mortality of rats treated orally with OCBC

Dose (mg/kg)	Number of deaths: Hours 0-4 M/F	Days 1 M/F	2 M/F	3 M/F	4-14 M/F	Total M/F
280	0/0	0/0	0/0	0/0	0/0	0/0
390	0/0	0/3	0/0	0/0	0/0	0/3
540	0/0	5/5	-/-	-/-	-/-	5/5
760	0/0	5/5	-/-	-/-	-/-	5/5

Test condition: Five males and five females (body weight 180 - 300 g) were used for each dose group. Animals were individually housed in wire mesh cages under 12-h light and12-h dark cycle condition. Other conditions were set according to AAALAC Standards. Commercial laboratory feed and water were freely given except for approximately 16 to 22 hours prior to the treatment. Test substance was administrated in a single dose to animals by gavage at dose levels of 280, 390, 540, and 760 mg/kg. Following administration, obsevations were made three times at the first day and daily thereafter for 14 days. Any symptoms of toxicity of the animals were recorded. Necropsy was made on all dead animals. At 14 days all surviving animals are weighed, then they were sacrificed and necropsied. LD50 with 95% confidence limits was calculated according to the method of C. S. Weil, Biometrics 249 (1952).
Reliability: (2) valid with restrictions

Comparable to guideline study with acceptable restrictions
24-NOV-2004 (34)

5.1.2 Acute Inhalation Toxicity

Type: LC50
Species: rat
Strain: Wistar

Sex: male/female
No. of Animals: 60
Exposure time: 4 hour(s)
Value: = 2.8 mg/l

Method: OECD Guide-line 403 "Acute Inhalation Toxicity"
Year: 1987
GLP: yes
Test substance: other TS:- Source: HOECHST AG- Code: GLAC 405- Purity: >99%

Result: Mortality during observation period:

Dose (mg/l)	males	females	cumulative
0.587	0 / 5	0 / 5	0 / 10
1.548	1 / 5	2 / 5	3 / 10
1.648	3 / 5	2 / 5	5 / 10
2.716	1 / 5	1 / 5	2 / 10
5.268	3 / 5	3 / 5	6 / 10
5.723	5 / 5	5 / 5	10 / 10

Deaths occurred in between day 1 and day 44 post beginning of treatment.
LD50 values determined by Probit analysis were as follows.
LC50 males: 2.8 mg/l
LC50 females: 2.8 mg/l
LC50 cumulative: 2.8 mg/l

Clinical symptoms were gasping respiration, respiratory sounds, uncoordinated, ataxic and stilted gait, cyanosis, stupor, squatting posture, prone position, flanks pinched in, nose and lid margin red-encrusted, corneal opacity, and narrow palpebra fissure. Except two females of the 5.268 mg/l group and one male and one female of the 1.548 mg/l group which showed weak symptoms at day 56 and day 21 respectively, all surviving animals were free of symptoms between day 5 to 14 and had exceeded their primary weights.

Macroscopic examination of perished rats revealed red coloured lungs. Pulmonary section resulted in discharge of a clear fluid and of foam. Sporadically beige spots on liver and inflated small intestine were observed. Except the two females killed at day 56 none of the rats sacrificed at the end of the observation period showed any macroscopic abnormalities.

Test condition: 30 male and 30 female Wistar rats, about 8 weeks and 10 weeks old, respectively, were used. Average bodyweights on the day of exposure were 201 g (184 - 217g) for the males and 199 g (177 - 209 g) for the females. Rats were allocated to 1 of 6 dose groups, each of 5 males and 5 females and were housed 5 of same sex in Makrolon cages with softwood granulate material. All rats had free access to food and tap water. Room temperature of the holding room was maintained within the range of 20-24 degree C and the mean relative humidity was 50 +/- 20 %. Five groups of rats were exposed (mouth/nose only) continuously for 4 hour to test atmospheres containing aerosol of 0.587, 1.548, 1.648, 2.716, 5.268 or 5.723 mg/l o-chlorobenzyl chloride (OCBC). The rats were observed during exposure and at least twice daily throughout the 14-day observation period. During the observation period all rats were weighed at day 7 and 14

post treatment. At the end of the 14-day observation period, the rats were sacrificed by an overdose of Nembutal except those animals which showed ongoing symptoms. Dead and sacrificed rats were subjected to a detailed macroscopic examination.
Reliability: (1) valid without restriction
OECD Guideline study
Flag: Critical study for SIDS endpoint
24-NOV-2004 (9)

Type: LC50
Species: rat
Strain: Wistar
Sex: male/female
No. of Animals: 20
Vehicle: no data
Exposure time: 1 hour(s)
Value: > 1.14 mg/l

Method: other
Year: 1987
GLP: yes
Test substance: other TS:- Source: Occidental Chemical Corpotration- Batch No.: DR2-11-85- Purity: 99.25%

Remark: The method was in principle equivalent to OECD Guideline 403, except that only one concentration of exposure was used and the duration of exposure was 1 hour.
Result: No animal death was observed at 1.140 mg/l during 14-day observation period. Many signs of irritation of respiratory tract were observed during exposure. The signs observed were piloerection, wetness and redness around the eyes, partial closing of the eyes, fluid discharge from the mouth, peripheral vasodilation, exaggerated respiratory movements and excessive activity. During observation period, signs observed were wet fur around the jaws, lethargy, peripheral vasodilatation and exaggerated respiratory movements. All rats were recoverd 5days after exposure. There were no macroscopic abnormalities and no histopathological changes that could be attributed to inhalation of OCBC vapour in any of the rats.
Test condition: Ten male and ten female Wistar rats, about 6 weeks and 8 weeks old respectively, were used. These ages of rats were selected so that males and females would be of similar body weight (ca. 200 g) on the day of exposure. Rats were allocated to 1 of 2 groups, each of 5 males and 5 females and were housed 5 of same sex to a suspended polypropylene cage with detachable wire mesh tops and floors. All rats had free access to a measured excess amount of food and tap water. The rats remained in a holding room except for the 1-hour exposure and an overnight post exposure period when they were kept in ventilated cabinet to allow dispersal of any residual test substance. One group of rats was exposed continously for 1 hour to a test atmosphere containing vapour of 1.140 mg/l OCBC, and another group as a control received clean air only for 1 hour. Room temperature was maintained within the range of 19-23 degree C and the mean relative humidity was 49%. The rats were observed during exposure and at least twice daily throughout the 14-day observation period. All rats were weighed daily from the day

of delivery to the laboratory until the end of the observation period. The amount of food and water consumed by each cage of rats was measured daily and the daily mean intakes of food and water for each rat were calculated from the recorded data. At the end of the 14-day observation period, the rats were anesthetised by intraperitoneal injection of pentobarbitone sodium and sacrified by exsanguination. The rats were subjected to a detailed macroscopic examination. The lung were removed and weighed in order to calculate the lung weight to bodyweight ratio. Histopathological examination was confined only to the lungs.

Reliability: (2) valid with restrictions
Comparable to guideline study with acceptable restrictions

28-JAN-2004 (34)

5.1.3 Acute Dermal Toxicity

Type:	LD50
Species:	rabbit
Strain:	New Zealand white
Sex:	male/female
No. of Animals:	30
Vehicle:	no data
Value:	= 1700 - 2200 ml/kg bw
Method:	other:FIFRA Pesticide Assessment Guidelines, Subdivision F, Section 81-2; "Acute Dermal Toxicity Study "TSCA Health Effects Test Guidelines; " Acute Exposure, Dermal Toxicity"
Year:	1986
GLP:	yes
Test substance:	other TS:-Source: Monsanto Company- Lot/Batch No.: 3168723, 2503577
Remark:	LD50

1900 mg/kg (95% confidence limits: 1287-2513 mg/kg)
male: 1700 mg/kg (95% confidence limits: 769-2631 mg/kg)
female: 2200 mg/kg (95% confidence limits: 1022-3378 mg/kg)
The method was in principle equivalent to OECD Guideline 402.

Result: No animal death was observed at 1000 mg/kg during 14-day observation period. Four males and two females died at 2000 mg/kg by Day 3, and all animals were dead at 4000 mg/kg by Day 7. The majority of animals at 2000 and 4000 mg/kg exhibited decreased activity and food consumption begininng 4 or 24 hours after administration. Other abnormalities seen in these groups, often as antemortem signs in animals which died, included ataxia, tremors, hypopnea, hypothermia, nasal discharge, unthrify coats and urinary and fecal staining. Survivors (in the 2000 mg/kg group) were free of signs of systemic toxicity by Day 10. The only systemic abnormalities seen in the 1000 mg/kg group were isolated occurrences of decreased activity and food consumption in one or two animals through Day 7. Most surviving animals exhibited severe dermal effects at the dose site (necrosis following by eschar formation, fissuring and/or exfoliation of the eschar tissue) which persisted throughout the study. Gross necropsies of animals founded dead revealed a number of

abnormalities (red foci and/or discoloration of lungs, white patches of liver, extremely large gall bladder, reddened or swollen uterus, testes found in body cavity, red walls of stomach and intestine and black foci in stomach walls), most of which appeared to represent postmortem autolytic changes. Observations in animals sacrificed at Day 14 confirmed the presence of dermal lesions (necrosis following by eschar formation, fissuring and/or exfoliation of the eschar tissue), and no other abnormalities related to administration were observed.

Test condition: Fifteen male and 15 female New Zealand rabbits, at least 8 weeks old at study initiation, were used. The rabbits weighed from 2.5 kg to 3.1 kg before administration. Rabbits were housed individually in the suspended stainless steel cages with wire mesh bottoms. The room temperature was maintained within the range of 60-70F and the relative humidity was maintained within the range of 30-70%. The lighting was provided for 12 hours per day. Food and water were freely suppled to the animals. One day before dosing, the hair of each rabbit was closely clipped from the dorsal area of the trunk with electric clipper, so as to expose at least 10% of the body surface area. Care was taken to avoid abrading the skin. Only animals with intact, healthy skin were used. The test substance was applied directly onto exposed skin of the animal at doses of 1000, 2000, and 4000 mg/kg, and spread evenly over the entire area. Guaze was then wrapped around the animal to cover the application site. The animal was then wrapped in an impervious plastic sleeve, designed to contain the test substance without leakage or undue pressure. The sleeve was secured with tape and Elizabethan collars were placed on all animals to prevent ingestion of the test substance or disruption of the wrappings. Animals were observed at approximately 1, 2, and 4 hours after application and daily thereafter for fourteen days. Gross necropsy was performed on all animals which died or were found dead during the study. All animals surviving at the end of the observation period were sacrificed and necropsied.

Reliability: (1) valid without restriction
Test procedure according to national standards (EPA)
Comparable to OECD guideline study

Flag: Critical study for SIDS endpoint

29-JAN-2004 (32)

Type: LD50
Species: rat
Strain: Sprague-Dawley
Sex: male/female
No. of Animals: 10
Vehicle: other:undiluted
Value: > 2000 mg/kg bw

Method: other
Year: 1993
GLP: yes
Test substance: other TS:- Source: Miki and Co., LTD- Lot No.: V1007- Purity : 99.64%

Method: EPA guidelines for registering Industrial Chemicals in the U.S., Pesticide Assessment Guidelines, Subdivision F,

Section 81-2, TSCA Health effects Test Guidelines, 40 CFR798.1100The Japanese Agricultural Chemicals Laws and Regulations Testing Guidelines for Toxicology Studies published by the Society of Agricultural Chemical Industry, under the auspices of MAFF (Ministry of Agriculture, Forestry and Fisheries).

Remark: Exposure time:24 hours
The method was in principle equivalent to OECD Guideline 402.

Result: There were no deaths during the study. Clinical findings noted for the majority of rats included clear ocular discharge, reddened extremities (nose, ears, forepaws), and urongenital staining. Soft stool and hypoactivity were observed for four and three rats, respectively. All animals appeared normal by day 3 or earlier. The test substance generally induced very slight to slight erythema and edema amd desquamation on all rats. Two sites had severe erythema, eschar and exfoliation. Multiple focal area of brown discoloration and white discoloration were noted for six and four application sites., respectively. Erythema and edema completely subsided by day 13 or earlier. Very slight body weight losses were noted for two females during the first week of the study and for one female during the second week of the study. There were no findings at the terminal necropsy. The LD50 of o-chlorobenzyl chloride was found to be greater than 2000 mg/kg when administered once for 24 hours to the shaved, intact skin of male and female rats.

Test condition: Animals were individually housed in suspended wire-mesh cages under 12-h light and 12-h dark cycle condition. Room temperature and humidity were maintained within the range of 70-75F and 28-52%. The room humidity was slightly below the guidelines specified range on one day. A brief period of decreased humidity would not be expected to adversely affect the health of the animals. Therefore, this deviation has no impact on the scientific validity, integrity or objective of this study. Commercial laboratory feed and water are freely available. On the day prior to dosing, the hair was removed from the backs of rats using a small animal clipper. One group concisting of five male and five female rats was dermally administered by a single dose (24-hour) at a dose level of 2000 mg/kg. Individual dosed of the undiluted test substance were applied to the dorsal skin using glass rod and covered approximately 16-20% of the total body surface. Doses were applied under gauze binders that were secured with Dermiform tape. Collars were applied and remained on the rats for the duration of the exposure period. Upon completion of exposure, the collars, bandages and residual test material were removed and the sites wiped with wet paper towels with tepid tap water. The rats were observed at approximately 1, 3 and 4 hours post-dose on day 0 and daily thereafter for 14 days. The application sites were examined for erythema, edema and other dermal findings beginning approximately 30-60 minutes after bandage removal and daily thereafter for thirteen days. The rats were shaved to facilitate dermal observations on study days 3, 7, 10 and 14. Body weights were recorded on days 0, 7 and 14. All animals surviving at the end of the observation period were sacrificed and necropsied.

Reliability: (1) valid without restriction

Test procedure according to national standards (EPA)
Flag: Critical study for SIDS endpoint
29-JAN-2004 (23)

5.1.4 Acute Toxicity, other Routes
-

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration: undiluted
Exposure: Semiocclusive
No. of Animals: 3
Result: slightly irritating

Method: OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year: 1992
GLP: yes

Method: "Test Guidelines and Criteria for Evaluating Dangerous Properties of Substances" (Maritime Tschology and Safety Breau, Ministry of Transport, Japan)
Result: No dermal reaction was observed immediately after patch removal in either application site exposed for 3 min, 60 min or 4 hr. From 24 hr to 7 days after patch removal, on the other hand, irritation reaction was observed in all the application sites. Slight dermal irritaion (erythema of Score 1) was observed in the 3 min-exposure sites, erythema of Score 1-2 in the 60-min exposure sites, and edema of Score 1 or 2 together with erythema in the 4-hr exposure sites. Thus increased exposure time tended to increase dermal reaction. The symptoms observed in all the application sites (3-min, 60-min and 4-hr exposure) in one animal (No. 1) disappeared within 7 days, and those in the other two animals within 10 days. In addition, scale was observed 7 or 10 days after application. Based on these results, it was concluded that o-chlorobenzyl chloride (OCBC) had no corrosion effect but had a slight dermal irritation potential on the rabbit skin.

Table 1.Scores of the skin reaction of the rabbit after application of OCBC at different times after patch removal.

Animal No.	Symptom	Time after patch removal: 3 min	60 min	4 hr	24 hr	48 hr	72 hr	7 d	10 d	14 d
1	erythema	0	-	-	1	1	0	0	0	0
	edema	0	-	-	0	0	0	0	0	0
	erythema	-	0	-	1	1	0	0	0	0
	edema	-	0	-	0	0	0	0	0	0
	erythema	-	-	0	2	2	1	0	0	0

	edema	-	-	0	2	1	0	0	0
2	erythema	0	-	-	1	1	1	1	0
	edema	0	-	-	0	0	0	0	0
	erythema	-	0	-	2	2	1	1	0
	edema	-	0	-	0	0	0	0	0
	erythema	-	-	0	2	2	1	1	0
	edema	-	-	0	2	1	0	0	0
3	erythema	0	-	-	1	1	1	1	0
	edema	0	-	-	0	0	0	0	0
	erythema	-	0	-	1	2	1	1	0
	edema	-	0	-	0	0	0	0	0
	erythema	-	-	0	1	2	1	1	0
	edema	-	-	0	2	2	0	0	0

Test condition: Exposure time:3, 60 minute(s) , 4 hour(s)
Test substance: as prescribed by 1.1 - 1.4-Source: Ihara Chemical Industry Co., Ltd.-Lot No.G44-4-Purity: 99.37%
Reliability: (1) valid without restriction
OECD Guideline study
Flag: Critical study for SIDS endpoint
25-NOV-2004 (21)

Species: rabbit
Concentration: undiluted
Exposure: Semiocclusive
Exposure Time: 4 hour(s)
No. of Animals: 3
Result: irritating

Method: OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year: 1985
GLP: yes
Test substance: other TS:- Source: HOECHST AG- Code: GLAC 405- Purity: >99%

Remark: EC classification:R38
Result: No necrosis was observed.

Animal No.	Symptom	Time after patch removal: 30-60 min	24 hr	48 hr	72 hr	7 d	14 d
1	erythema	1	3	3	4	2	0
	edema	4	1	1	1	0	0
2	erythema	1	3	3	3	1	0
	edema	3	1	1	1	0	0
3	erythema	1	2	2	2	2	0
	edema	2	2	1	1	0	0

These results have led to the conclusion that OCBC had no corrosion effect but had a dermal irritation potential on the rabbit skin under these study conditions.

Reliability: (1) valid without restriction
OECD Guideline study

24-NOV-2004 (8)

Species: rabbit
Concentration: undiluted
No. of Animals: 6
PDII: 3.9
Result: irritating

Method: other:FIFRA Pesticide Assessment Guidelines, Subdivision F, Section 81-5, "Primary Dermal Irritaion Study "TSCA Health Effects Test Guidelines, "Acute Exposure, Primary dermal Irritation"
Year: 1986
GLP: yes
Test substance: other TS:-Source: Monsanto Company-Lot/Batch No.: 3168723, 2503577

Remark: The method was in principle equivalent to OECD Guideline 404, except that the test substance was not removed (not rinsed) after the exposure period.
Result: (4-hour application)
Irritation at the 4 hours sites generally consisted of slight to moderate erythema and edema. No tissue destruction was seen, and two of the six animals were free at all irritation within 10 to 14 days after test substance application.

Table 1.Scores(a) of the skin reaction of the rabbit after application of OCBC at different times after patch removal.

Animal No.	Symptom	Time after patch removal: 0.5 hours	24 hours	48 hours	72 hours	7 days	10 days	14 days
1M	erythema	1	1	3	3	3	2	1
	edema	3	3	3	3	3	3	3
	erythema	1	2	3	3	3	2	1
	edema	3	3	3	3	3	3	3
2M	erythema	1	2	3	3	2	2	1
	edema	3	3	3	2	2	2	2
	erythema	1	2	3	3	3	2	1
	edema	3	3	3	2	2	2	2
3F	erythema	1	3	3	2	1	0	-
	edema	2	2	1	1	1	0	-
	erythema	1	2	3	2	1	0	-
	edema	2	2	1	1	0	0	-
4F	erythema	2	3	3	2	1	0	-
	edema	2	3	1	1	0	0	-
	erythema	2	3	3	2	1	1	1

	edema	2	3	1	1	0	0	0
5F	erythema	2	3	3	3	1	1	1
	edema	2	2	1	1	0	0	0
	desquamation	-	-	-	-	x	x	x
	erythema	1	3	2	1	1	1	1
	edema	2	2	1	1	0	0	0
	desquamation	-	-	-	-	-	x	-
6M	erythema	1	2	2	2	2	1	0
	edema	2	3	2	2	1	0	0
	erythema	1	2	2	2	2	1	0
	edema	1	3	2	2	1	0	0

(a): Scored using scale presented in Table 3.
-: Observation not present
x: Observation present
F: female; M: male

(24-hour application)
Four of the six animals had blanching of the skin, generally with moderate to severe edema, through 72 hours. The other two animals had slight to severe erythema and edema. Five of the animals subsequently exhibit epidermal or subepidermal tissue damage. The primary irritation index for the 24-hour exposure was 3.9. However, this low number reflects the blanching (and consequent absence of erythema scores) in most animals through 72 hours.

Table 2.Scores(a) of the skin reaction of the rabbit after application of OCBC at different times after patch removal.

Animal No	Symptom	Time after patch removal: 24.5 hours	48 hours	72 hours	7 days	10 days	14 days
1M	erythema	0b	0b	0b	2	3	4
	edema	4	3	3	2	3	3
	superficial necrosis	-	-	-	-	-	x
	erythema	0b	0b	0b	3	4	4
	edema	4	3	3	3	3	3
	superficial necrosis	-	-	-	-	x	-
	desquamation	-	-	-	-	-	x
	necrosis	-	-	-	-	-	x
	eschar	-	-	-	-	-	x
	subepidermal damage	-	-	-	-	-	x
2M	erythema	0b	0b	0b	3	4	4
	edema	4	3	3	3	3	3
	necrosis	-	-	-	-	x	x
	erythema	0b	0b	0b	3	4	4

	edema	4	3	3	3	3	3
	superficial necrosis	-	-	-	-	x	x
	desquamation	-	-	-	-	-	x
3F	erythema	0b	0b	0b	2	4	4
	edema	4	2	1	2	2	2
	superficial necrosis	-	-	-	-	x	x
	desquamation	-	-	-	-	-	x
	necrosis	-	-	-	-	-	x
	lack of hair regrowth	-	-	-	-	-	x
	subepidermal damage	-	-	-	-	-	x
	erythema	0b	0b	0b	2	4	4
	edema	4	2	1	1	1	1
	superficial necrosis	-	-	-	-	x	-
	necrosis	-	-	-	-	-	x
	eschar	-	-	-	-	-	x
	exfoliation	-	-	-	-	-	x
	subepidermal damage	-	-	-	-	-	x
4F	erythema	0b	0b	0b	2	2	1
	edema	4	2	1	1	1	1
	desquamation	-	-	-	-	-	x
	erythema	0b	0b	0b	4	4	4
	edema	4	2	2	2	2	2
	superficial necrosis	-	-	-	x	x	-
	necrosis	-	-	-	-	-	x
	eschar	-	-	-	-	-	x
	exfoliation	-	-	-	-	-	x
	lack of hair regrowth	-	-	-	-	-	x
	subepidermal damage	-	-	-	-	-	x
5F	erythema	0b	4b	4b	4	4	4
	edema	4	2	2	2	2	2
	superficial necrosis	-	x	x	x	-	-
	necrosis	-	-	-	-	x	x
	exfoliation	-	-	-	-	-	x
	lack of hair regrowth	-	-	-	-	-	x
	scarring	-	-	-	-	-	x
	subepidermal damage	-	-	-	-	-	x
	erythema	4	4	4	4	4	4
	edema	4	3	3	2	2	2
	necrosis	x	x	x	x	x	x
	eschar	-	-	-	x	x	x
	exfoliation	-	-	-	-	-	x
	subepidermal						

	damage	-	-	-	-	-	x
6M	erythema	1	2	2	3	2	1
	edema	4	2	2	2	1	1
	erythema	1	2	2	3	2	1
	edema	4	3	3	2	2	2

a: Scored using scale presented in Table 3.
b: Blanched
-: Observation not present
x: Observation present
F: female; M: male

Test condition: Exposure:semi-occlusive (4 hour), occlusive (24 hr)
Exposure time:4, 24 hour(s)
Three male and female young adult New Zealand White rabbits were used. Rabbits were housed individually in the suspended stainless steel cages under a 12-h light and12-h dark cycle. Food and water was freely available at all times. The room temperature and relative humidity were maintained within the range of 60-70F and 30-70%, respectively. One day before dosing, the hair of each rabbits was closely clipped from the dorsal area of the trunk with an electric clipper, so as to expose at least 10% of the body surface area. The test substance was applied to two intact sites on each animal. The 0.5 ml of the test substance was applied beneath a gauze square, 1"x1", placed directly on each of two test sites nearest the head of rabbits and held in place with non-irritating tape. Gauze was then wrapped around the animal and covered with porous tape, to semi-occlude the test sites. Following 4 hours (semi-occlusive) or 24 hours (occlusive) of exposure, the wrapping and gauze square were removed. Observations of test sites were made for all animals at 30 minutes, 24, 48, and 72 hours after 4-hour exposure and at 24.5, 48 and 72 hours after 24-hour exposure. If there were any signs of irritation noted at the 72 hour observation, observations were made at each affected site 7, 10 and 14 days after treatment or until no signs of irritation were present. Each site was treated independently, i.e., if irritation was no longer present at a site at 72 hours or any interval thereafter, no further scoring was performed on that site. At each interval, all sites were evaluated for erythema and edema or other evidence of dermal irritation according to the Draize scoring system (See Table 3). The most affected area was scored. Adjacent areas of untreated skin were used for comparison.

Table 3.Draize evaluation of dermal irritation

Erythema and eschar formation	Grade
No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness), eschar (scab) formation or necrosis	4
Edema formation	
No edema	0

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                    Very slight edema (barely perceptible)          1
                    Slight edema (edges of area well-defined
                         by definiterasing)                         2
                    Moderate edema (raised approximately 1 mm)      3
                    Severe edema (raised more than 1 mm and
                         extending beyond area of exposure          4

               Other signs
                    Desquamation - Scaling or flaking of epidermal tissue
                    (not including scabs or necrotic areas)
                    Exfoliation - Sloughing of dead (necrotic) tissue
                    and or scabs (eschar)
                    Lack of hair regrowth
                    Scarring
                    Eschar (scab formation)
                    Necrosis (presence of dead tissue)
               ========================================================
Reliability:   (1)  valid without restriction
               Test procedure according to national standards (EPA)
24-NOV-2004                                                          (32)

Species:       rabbit
Concentration: undiluted
Exposure:      Occlusive
Exposure Time: 4 hour(s)
No. of Animals: 6
PDII:          3.5
Result:        moderately irritating

Method:        other:DOT Skin Corrosivity, 49 CFR 173.240
  Year:        1984
   GLP:        yes
Test substance: other TS:- Source: Occidental Chemical Corporation

Remark:        The method was in principle equivalent to OECD Guideline
               404, except that the dermal responses were scored at 4, 24
               and 48 hours after application.
Result:        No necrosis was observed. All animals had very slight to
               slight edema and exhibited well-defined erythema through 48
               hours. The primary irritation index was calculated to be
               3.5. These results have led to the conclusion that
               orthochlorobenzyl chloride was found to be moderate
               irritating to the skin but not corrosive.

               Table 1.Scores of the skin reaction of the rabbit after
               application of OCBC at different times after patch removal.
               ============================================
               Animal   Symptom  Time after application
               No.               ----------------------
                                 4     24    48
                                 hours hours hours
               ------------------------------------------------
               1     erythema    2     2     2
                     edema       2     1     1
               ------------------------------------------------
               2     erythema    2     2     2
                     edema       2     1     1
               ------------------------------------------------
               3     erythema    2     2     2
                     edema       2     1     1
```

4	erythema	2	2	2
	edema	2	2	1
5	erythema	2	2	2
	edema	2	2	1
6	erythema	2	2	2
	edema	2	2	1

Test condition: Six male or female New Zealand rabbits, weighed over 2.0 kg, were used. The rabbits were housed individually in elevated wire mesh cages under a 12-h light: 12-h dark cycle. Commercial laboratory feed and water was freely available at all times. Other conditions were according to AAALAC standards. The hair was removed from an area of the back and side of each animal using a small animal clipper. The 0.5 mL of test substance was applied to one intact skin site on each rabbit and covered with a piece of gauze (not less than 1 inch x 1 inch and 2 ply thick). The gauze was secured with tape and trunk of the animal was wrapped with a rubber dam.
The animals were harnessed. At 4-hours, the patches and harnesses were removed. At the time of patch removal, the test sites were evaluated for corrosively, and also observed at 24 hours (20 hours after patch removal) and at 48 hours (44 hour after patch removal). In addition, the skin was graded according to the Draize technique (See Table 2) at 4, 24, and 48 hours

Table 2.Draize evaluation of dermal irritation

Erythema and eschar formation	Grade
No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness), eschar (scab) formation or necrosis	4

Edema formation	
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well-defined by definite rasing)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure	4

Reliability: (2) valid with restrictions
Comparable to gudeline study with acceptable restrictions
25-NOV-2004 (34)

5.2.2 Eye Irritation

Species: rabbit
Concentration: undiluted
Dose: .1 ml
Exposure Time: 24 hour(s)

Comment: other:rinsed with physiological saline
No. of Animals: 3
Result: slightly irritating

Method: OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year: 1985
GLP: yes
Test substance: other TS:- Source: HOECHST AG- Code: GLAC 405- Purity: >99%

Result: All animals gave positive responses. Beside the numerical grades of ocular reactions displayed in the table beneath animals excrete a clear liquid at the day of application. All symptoms were completely reversible within the observation period.

Numerical grades of ocular reactions after treatment

Animal No.	Region	Time after application: 1 hr	24 hr	48 hr	72 hr	7 d	14 d
1	Conjunctivae						
	-Chemosis	2	1	0	0	0	0
	-Redness	2	1	1	0	0	0
	Iris	1	0	1	0	0	0
	Cornea	0	0	2	0	0	0
2	Conjunctivae						
	-Chemosis	2	2	1	1	1	0
	-Redness	2	3	2	2	2	0
	Iris	1	1	1	0	0	0
	Cornea	0	1	2	0	0	0
3	Conjunctivae						
	-Chemosis	2	1	0	0	0	0
	-Redness	2	2	1	0	0	0
	Iris	1	0	1	0	0	0
	Cornea	0	0	2	0	0	0

These results have led to the conclusion that OCBC had only slight eye irritant effects which do not meet criteria for classification and labelling according to EC regulations.
Reliability: (1) valid without restriction
OECD Guideline study
Flag: Critical study for SIDS endpoint
25-NOV-2004 (7)

Species: rabbit
Concentration: undiluted
Dose: .1 ml
Comment: not rinsed
No. of Animals: 6

Method: other:FIFRA Pesticide Assessment Guidelines, subdivision F, Section 81-4, "Primary Eye Irritation Study" TSCA Health Effects Test Guidelines, "Acute Exposure, Primary Eye Irritation"
Year: 1986
GLP: yes
Test substance: other TS:- Source: Monsanto company- Lot/Batch No.: 3168723,

2503577

Remark: The method was in principle equivalent to OECD Guideline 405.

Result: mildly/moderately irritating

OCBC produced mild to moderate but reversible ocular irritation. All six animals exhibited slight to moderate conjunctival irritation (redness, chemosis, discharge), three exhibited corneal opacity and ulceration and one had iridial damage. However, six animals were free of significant ocular irritation within 3 to 21 days after instillation of the test material.

Table 1.Numerical grades awarded to the ocular reactions elicited by OCBC

Animal No.	Region of eye	Time after application						
		1h	24h	48h	72h	7d	14d	21d
1	Conjunctivae							
	Redness	1	1	1	1	0	ND	ND
	Chemosis	1	1	1	1	0	ND	ND
	Discharge	2	0	0	0	0	ND	ND
	Necrosis(N)/ Ulceration(U)	0	0	0	0	0	ND	ND
	Iris	+	0	0	0	0	ND	ND
	Cornea							
	Opacity	0	0	0	0	0	ND	ND
	Area	0	0	0	0	0	ND	ND
	Stipping	0	0	0	0	0	ND	ND
	Ulceration	0	0f	0f	0	0	ND	ND
	Other	-	-	-	-	-	ND	ND
2	Conjunctivae							
	Redness	1	3	2	2	0	ND	ND
	Chemosis	1	1	1	1	0	ND	ND
	Discharge	2	1	0	0	0	ND	ND
	Necrosis(N)/ Ulceration(U)	0	0	0	0	0	ND	ND
	Iris	+	+	+	0	0	ND	ND
	Cornea							
	Opacity	0	2	1	+	0	ND	ND
	Area	0	4	4	4	0	ND	ND
	Stipping	0	0	0	0	0	ND	ND
	Ulceration	0	1f	0f	0f	0	ND	ND
	Other	-	-	-	-	-	ND	ND
3	Conjunctivae							
	Redness	1	1	1	2	1	1	1
	Chemosis	1	1	1	1	0	0	0
	Discharge	2	0	0	0	0	0	0
	Necrosis(N)/ Ulceration(U)	0	0	0	0	0	0	0

	Iris	+	+	0	0	0	0	0
	Cornea							
	Opacity	+	0	0	0	0	0	0
	Area	2	0	0	0	0	0	0
	Stipping	0	0	0	0	0	0	0
	Ulceration	0	0f	0f	0	0	0	0
	Other	-	-	-	-	-	0	0
4	Conjunctivae							
	Redness	1	2	1	1	0	ND	ND
	Chemosis	1	1	1	1	0	ND	ND
	Discharge	3	0	0	0	0	ND	ND
	Necrosis(N)/ Ulceration(U)	0	0	0	0	0	ND	ND
	Iris	0	1	0	0	0	ND	ND
	Cornea							
	Opacity	+	1	+	+	0	ND	ND
	Area	2	4	4	4	0	ND	ND
	Stipping	0	1	0	0	0	ND	ND
	Ulceration	0	1f	0f	0f	0	ND	ND
	Other	-	-	-	-	-	ND	ND
5	Conjunctivae							
	Redness	1	2	1	1	1	0	ND
	Chemosis	2	1	1	1	1	0	ND
	Discharge	2	0	1	0	0	0	ND
	Necrosis(N)/ Ulceration(U)	0	0	0	0	0	0	ND
	Iris	0	+	0	0	0	0	ND
	Cornea							
	Opacity	+	1	+	+	0	0	ND
	Area	2	4	4	4	0	0	ND
	Stipping	1	1	1	0	0	0	ND
	Ulceration	0	1f	0f	0f	0	0	ND
	Other	-	-	-	-	-	-	ND
6	Conjunctivae							
	Redness	1	2	2	1	0	0	ND
	Chemosis	1	1	1	1	1	0	ND
	Discharge	2	1	0	0	0	0	ND
	Necrosis(N)/ Ulceration(U)	0	0	0	0	0	0	ND
	Iris	+	0	0	0	0	0	ND
	Cornea							
	Opacity	+	0	0	0	0	0	ND
	Area	2	0	0	0	0	0	ND
	Stipping	0	0	0	0	0	0	ND
	Ulceration	0	0f	0f	0	0	0	ND
	Other	-	-	-	b	-	-	ND

b - one small area of superficial necrosis on lower lid.
f - observation confirmed with fluorescein.
ND- no dat

Test condition: Grading and scoring of irritation were performed in accordance with the following table:

Table 2

### CORNEA ###	
A. Opacity-degree of density (area most dense taken for reading)	Grade
- No opacity	0
- Slight dulling of normal luster	+
- Scattered or diffuse areas of opacity (other than slight dulling of normal luster), details of iris clearly visible	1
- Easily discernible translucent areas, details of iris slightly obscured	2
- Nacreous areas, no details of iris visible, size of pupil barely discernible	3
- Opaque cornea, iris not discernible through the opacity	4
B. Total area of cornea involved: (total area exhibiting any opacity, regardneless of degree)	Grade
- One quarter (or less) but not zero	1
- Greater than one quarter less than half	2
- Greater than half, but less than three quarters	3
- Greater than three quarters, up to whole area	4
C. Stippling - (appearance of pinpoint roughening)	Grade
- No stippling	0
- One quarter (or less) but not zero	1
- Greater than one quarter less than half	2
- Greater than half, but less than three quarters	3
- Greater than three quarters, up to whole area	4
D. Ulceration -(absence of a gross patch of corneal epithelium)	Grade
- No ulceration	0
- One quarter (or less) but not zero	1
- Greater than one quarter less than half	2
- Greater than half, but less than three quarters	3
- Greater than three quarters, up to whole area	4

### IRIS ###	
A. Values	Grade
- Normal	0
- Slight deepining of the rugae or slight hyperemia of the circumcorneal blood vessels	+
- Markedly deepened rugae, congestion, swelling, moderate circumcorneal hyperaemia or injection, any of these or combination of any therof, iris still reacting to light (sluggish reaction is positive)	1
- No reaction to light, hemorrhage, gross destruction (any one or all of these)	2

### CONJUNCTIVAE ###	
A. Redness (refers to palpebral and bbulbar conjunctivae excluding cornea and iris)	Grade
- Vessels normal	0
- Some vessels definitely injected above normal	1
- Diffuse, crimson red, individual vessels not easily discernible	2
- Diffuse beefy red	3
B. Chemosis	Grade
- No swelling	0
- Any swelling above normal (includes nictitating membrane)	1
- Obvious swelling with partial eversion of the lids	2
- Swelling with lids about half closed	3
- Swelling with lids more than half closed	4
C. Discharge	Grade
- No discharge	0
- Any amount different from normal (does not include small amount observed in inner canthus of normal animals)	1
- Discharge with moistening of the lids and hairs just adjacent to the lids	2
- Discharge with moistening of the lids and hairs and considerable area around the eye	3
D. Necrosis or ulceration of palpebral and bulbar conjunctivae	Grade
- Not present	0
- Necrosis present	N
- Ulceration present	U

Reliability: (1) valid without restriction
Test procedure according to national standards (EPA)
Flag: Critical study for SIDS endpoint
25-NOV-2004 (32)

Species: rabbit
Concentration: undiluted
Dose: .1 ml
Exposure Time: .5 minute(s)
Comment: other:rinsed with water for one minute
No. of Animals: 4
Result: irritating

Method: other:Federal Register, vol.50, No.188, part II of 27 September 1985 Section 798.4500 - Primary Eye Irritation
Year: 1987
GLP: yes
Test substance: other TS:-Source: Occidental Chemical Corporation-Batch No.:DR2/11/85- Purity: 99.25%

Remark: The method was in principle equivalent to OECD Guideline

405, except that the eyes were irrigated 30 seconds after instillation with water for one minute.

Result: (With rinsing)
Three animals gave a positive response. No corneal damage or iridal inflammation was seen in any of the animals. Obvious swelling with partial eversion of the eyelids was observed in all three animals one hour after instillation only. The eyes were normal, 2, 3, or 4 days after instillation.

Table 1.Numerical grades awarded to the ocular reactions elicited by OCBC (1).

Animal No.	Region of eye	Time after application					
		1h	1d	2d	3d	4d	7d
1	Cornea	0	0	0	0	0	0
	Iris	0	0	0	0	0	0
	Conjunctivae						
	-Redness	1	1	1	0	0	0
	-Chemosis	2	0	1	0	0	0
2	Cornea	0	0	0	0	0	0
	Iris	0	0	0	0	0	0
	Conjunctivae						
	-Redness	1	1	0	0	0	0
	-Chemosis	2	1	0	0	0	0
3	Cornea	0	0	0	0	0	0
	Iris	0	0	0	0	0	0
	Conjunctivae						
	-Redness	1	0	1	1	0	0
	-Chemosis	2	0	1	0	0	0

(Without rinsing)
The animal gave a positive response. A corneal opacity developed 24 hours after instillation and persisted through Day 14. Iridial inflammation was observed between one and three days after instillation. A diffuse crimson coloration of the conjunctivae, accompanied by considerable swelling with the eyelids about half-closed and a copious discharge was observed in the animal. All effects were reversible within the observation period of 21 days.

Table 2.Numerical grades awarded to the ocular reactions elicited by OCBC (2).

Animal No.	Region of eye	Time after application							
		1h	1d	2d	3d	4d	7d	14d	21d
1	Cornea	0	1	2	2	2	2	1	0

Iris	0	1	1	1	0	0	0	0
Conjunctivae								
-Redness	2	2	2	2	1	1	1	0
-Chemosis	2	3	3	1	2	1	0	0

Test condition: Number of animals:4 (with rinsing:3, without rinsing:1)

OCBC (0.1 ml) was applied to eyes of 4 rabbits. The eyes of 3 rabbits were rinsed with water for one minute after 30-second exposure while the eye of one rabbit was not rinsed during the experiment.

Grading and scoring of irritation were performed in accordance with the following table:

Table3

### CORNEA ###	
Opacity-degree of density (area most dense taken for reading)	Grade
- No ulceration opacity	0
- Scattered or diffuse areas of opacity (other than slight dulling of normal luster), details of iris clearly visible	1
- Easily discernible translucent areas, details of iris slightly obscured	2
- Nacreous areas, no details of iris visible, size of pupil barely discernible	3
- Opaque cornea, iris not discernible through the opacity	4

### IRIS ###	
	Grade
- Normal	0
- Markedly deepened rugae, congestion, swelling, moderate circumcorneal hyperaemia or injection,any of these or combination of any therof, iris still reacting to light (sluggish reaction is positive)	1
- No reaction to light, hemorrhage, gross destruction (any one or all of these)	2

### CONJUNCTIVAE ###	
A. Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris)	Grade
- Blood vessels normal	0
- Some blood vessels definitely hyperaemic	1
- Diffuse, crimson colour, individual vessels not easily discernible	2
- Diffuse, beefy red	3

B. Chemosis	Grade
- No swelling	0
- Any swelling above normal (includes nictitating membrane)	1
- Obvious swelling with partial eversion of the lids	2
- Swelling with lids about half-closed	3
- Swelling with lids more than half-closed	4

Reliability: (1) valid without restriction
Comparable to guideline study
25-NOV-2004 (34)

5.3 Sensitization

Type: other:Skin sensitization test
Species: guinea pig
No. of Animals: 13
Vehicle: other:olive oil
Result: sensitizing

Method: other
Year: 1936
GLP: no data
Test substance: other TS

Result: Positive skin reaction was observed in eight of thirteen animals. Animals sensitized with OCBC were also cross-reacted with 2,4-dinitrobenzyl chloride.
Test condition: Thirteen guinea pigs were intracutaneously injected with 0.01mg o-chlorobenzyl chloride (OCBC), twice a week for 12 weeks, followed by two weeks of rest. Then one drop of 20% orthochlorobenzyl chloride solution in olive oil was spread on the flank.
Reliability: (3) invalid
Does not meet important criteria of today standard methods.
29-JAN-2004 (26)

5.4 Repeated Dose Toxicity

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of administration: gavage
Exposure period: male: 45 days, female: 41-48 days
Frequency of treatment: daily
Doses: 2, 10, 50 mg/kg/day
Control Group: yes
NOAEL: = 2 mg/kg

Method: OECD combined study TG422
Year: 1999
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Result: Suppression of body weight gain and decrease in food consumption were observed in both sexes in the early period of administration at 50 mg/kg/day. At necropsy, thickening

of the forestomach wall was observed in males of 10 mg/kg/day and both sexes of 50 mg/kg/day. The relative liver weight was increased and absolute liver weight tended to be increased in females of 50 mg/kg/day. Histopathological examination revealed squamous epithelium hyperplasia, erosion and ulceration in the forestomach in males of 10 mg/kg/day and both sexes of 50 mg/kg/day. These changes observed in the forestomach were considered to be related to the irritancy of test substance. In addition, the increase of hyaline droplets in the proximal tubular epithelium, eosinophilic bodies, granular casts and basophilic tubule were observed in the kidneys of males of 50 mg/kg/day. There were no effects on hematological and clinical examination or organ weights in males. In this experiment, the no observed effect level (NOEL) was considered to be 2 mg/kg/day for male and 10 mg/kg/day for female.

Table 1. Absolute and relative liver weights in rats treated orally with OCBC(a)

Dose (mg/kg)			
0	2	10	50
[Male]			
No. of animals			
12	12	12	12
Body weight (g)			
464+/-30	478+/-27	457+/-19	461+/-27
Liver, absolute (g)			
12.2+/-1.4	12.6+/-1.1	11.7+/-1.0	12.4+/-1.5
Liver, relative (g%)			
2.62+/-0.19	2.64+/-0.12	2.55+/-0.17	2.69+/-0.20
[Female]			
No. of animals			
12	11	11	11
Body weight (g)			
324+/-26	314+/-29	302+/-25	313+/-15
Liver, absolute. (g)			
13.6+/-1.7	13.9+/-1.5	13.2+/-1.6	14.6+/-1.0
Liver, relative (g%)			
4.21+/-0.32	4.43+/-0.34	4.37+/-0.28	4.67+/-0.23**

Values are expressed as Mean+/-S.D.
Significantly different from control;**: P<0.01
(a)No significant change was observed in absolute nor relative weights of the following organs; thymus, spleen, kidneys, adrenals, testes, and epididymis.

Test condition: Nine-week-old male and female rats were used. Twelve males and twelve females were used for each dose levels, 2, 10, and 50 mg/kg/day. 0.1% Tween 80 solution was gavaged control group. Test substance was administrated by gavage. Males

were dosed for 14 days before mating; during the mating period and up to the day before scheduled kill (total 45 days). Females were dosed for 14 days before mating, during the mating period, during the gestation and four days after delivery (total 41-48 days). The rats were weighed at Day 3, 7 and 14, and weekly thereafter. During the gestation, females were weighed at Day 0. 7, 14 and 20 of gestation, and Day 0 and 4 of lactation. At the termination of the experiment, all rats were sacrificed and necropsied. Hematological examination and clinical biochemistry determination were performed on the blood samples obtained from the male rats. Histopathological examinations by hematoxylin eosin staining were carried out on brain, stomach, heart, liver, kidneys, spleen, adrenals, testes and epididymides of the all animals in the control and 50 mg/kg/day group, and on all gross lesions of all animals. The treatment-related changes were observed in the kidney of 50 mg/kg/day, therefore, histpathological examination were performed on the kidney of all animals in 2 and 10 mg/kg/day group.

Test substance: -Source: Ihara Chemical Industry Co., Ltd.-Lot No.T7030-Purity: 99.65%

Reliability: (1) valid without restriction
OECD Guideline study

Flag: Critical study for SIDS endpoint

25-NOV-2004 (28)

Species: rat Sex: male/female
Strain: Wistar
Route of administration: inhalation
Exposure period: 28 days
Frequency of treatment: 6 hours a day, five consecutive days a week (Monday to Friday) for 4 consecutive weeks
Doses: 0.01, 0.03, 0.10 mg/l
Control Group: yes
NOAEL: = .03 mg/l

Method: OECD Guide-line 412 "Repeated Dose Inhalation Toxicity: 28-day or 14-day Study"
Year: 1990
GLP: yes
Test substance: other TS:- Source: Occidental Chemical Corporation-Batch No.:20-50253 00/S-2359- Purity: 99%

Result: No animals were dead. At the highest exposure level only, there were several observations indicative of an adverse effect of the test substance. During exposure, there were clinical signs indicative of an irritation of the respiratory tract. These included eyes shut/half-shut, adoption of a prone/hunched posture, rubbing of the chin on the mesh floor of the exposure chamber with licking of the inside of the mouth, red ears, agitated grooming and short periods of head shaking, and rale was noted in one male rat of highest dose group during the latter half of Week 4. Weight gain, food consumption and water consumption were reduced during the 4 weeks of exposure. The laboratory investigations performed at the end of the exposure period showed increased packed cell volume, hemoglobin and red cell count and production of a reduced volume of urine. The ratio

of myeloid: erythroid cells was also increased. The gross necropsy revealed enlarged tracheobronchial lymph nodes and elevated lung weights. The histopathological examination showed damage to the nasal mucosa, trachea and bronchi (epithelial degeneration and hyperplasia of the nasal mucosa and the bronchiolar epitherium, squamous metaplasia of the bronchiolar epitherium) consistent with inhalation of an irritant vapour. The tracheobronchial lymph nodes of some of the rats showed lymphoid hyperplasia. There were no changes that were considered to be treatment-related in male and female rats exposed at 0.01 or 0.03 mg/l. The no observed adverse effect level (NOAEL) in this study was considered to be 0.03 mg/l.

Table 1. Effects of OCBC observed in the lungs

Dose (mg/l)	0	0.01	0.03	0.10
[Male]				
No. of animals	5	5	5	5
Body weight (g)	392	384	380	306
Weight gain (g)	131	127	127	52**
Lung weight (g)	1.37	1.37	1.38	1.47
Enlarged tracheo-bronchial lymph nodes	0	0	0	4
Lymphoid hyperplasia in tracheo-bronchial lymph node	0	0	0	3
[Female]				
No. of animals	5	5	5	5
Body weight (g)	244	231	234	224
Weight gain (g)	61	53	50	33**
Lung weight (g)	1.04	1.07	1.05	1.25**
Enlarged tracheo-bronchial lymph nodes	0	0	0	1
Lymphoid hyperplasia in tracheo-bronchial lymph node	0	0	0	1

**, P<0.01 compared with control data using Williams' test

Test condition: Both male and female rats, 6 weeks old, were used. Five males and five females were used for each dose levels. Rats were whole-body exposured to the atmosphere containing vapour of the test substance, 6 hours a day, five consecutive days a week (Monday to Friday) for 4 consecutive weeks, and the concentrations of o-chlorobenzyl chloride were 0.01, 0.03, and 0.10 mg/l. Clinical signs during exposure were recorded. Animals were examined twice each day, usually prior to loading and immediately following unloading from the chambers on exposure days, and in the morning and afternoon on non-exposure days. Each rat was weighed daily, and food and water consumption were also recorded daily.Samples of blood used for hematological and biochemical examinations were withdrawn from the orbital sinus of each rat during Week 4 of the study. The rats were lightly anaesthetized with ether during removal of blood. No food was available to the rats overnight prior to sampling. Urine was collected from all rats overnight. All rats in all groups were sacrificed and necropsied. At necropsy, samples of bone marrow were removed from the femur of all rats and

the ratio of myeloid: erythroid cells present was calculated for each rat. Histopathological examinations were performed on the nasal passages, pharynx, larynx, trachea, lungs, liver, spleen, heart, kidneys, adrenals, and any gross abnormalities in all rats in control and the 0.01 mg/l group. As a result of findings in the 0.1 mg/l group, the trachea, nasal turbinate, larynx, tracheobronchial lymph nodes and lungs were also examined in the 0.01 and 0.03 mg/l group.

Reliability: (1) valid without restriction
OECD Guideline study
Flag: Critical study for SIDS endpoint
25-NOV-2004 (33)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella typhimurium TA100, TA1535, TA98, TA1537, Escherichia coli WP2 uvrA
Concentration: 0.0156 - 0.5 mg/plate
Cytotoxic Concentration: without metabolic activation:
>0.25 mg/plate(S. typhimurium TA1535,TA98,TA1537,E. coli WP2uvrA)
>0.18 mg/plate (S. typhimurium TA100)
with metabolic activation:
>0.25 mg/plate(S. typhimurium TA,100, TA1535, TA98, TA1537, E. coli WP2 uvrA)
Metabolic activation: with and without

Method: OECD Guide-line 471
Year: 1999
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Result: possibly positive

In S. typhimurium TA100, concentration-related increases of the number of revertant colonies were observed reproducibly without metabolic activation, but number of revertant colonies was not twice as many as that of the solvent control. Therefore, follow-up tests and a verification test were performed at 0.09 to 0.24 mg/plate in S. typhimurium TA100 without metabolic activation. The results of these tests revealed concentration-related increases of the number of revertant colonies, and the number of revertant colonies was from1.5 to 2.1-times as many as that of the solvent control. These results have led to the conclusion that OCBC was possibly mutagenic in S. typhimurium TA100 without metabolic activation. No mutagenic activity was observed in S. typhimurium TA1535, TA98, TA1537 and E. coli WP2 uvrA both with and without metabolic activation, and in S. typhimurium TA100 with metabolic activation.

Table 1.Mutagenicity of OCBC on bacteria (1)

With or without S9mix	Test substance dose (ug/plate)	Mean number of revertant colonies/plate	
		Base-pair	Frameshift

		substitution type		frameshift type		
		TA 100	TA 1535	WP2 urvA	TA 98	TA 1537
without (-)	0	125	9	24	22	7
	15.6	142	10	26	16	7
	31.3	169	11	21	22	8
	62.5	194	9	25	24	9
	125	205	10	25	26	10
	250	0*	0*	1*	0*	1*
	500	0*	0*	0*	0*	0*
with (+)	0	142	11	33	33	13
	15.6	127	12	33	23	12
	31.3	166	10	33	36	14
	62.5	159	12	32	28	15
	125	172	10	32	32	13
	250	68*	6*	35	21*	8*
	500	0*	1*	0*	3*	0*
[Positive control without S9mix]						
Chemical		AF2	SA	AF2	AF2	9AA
Dose(ug/plate)		0.01	0.5	0.01	0.1	80
Mean number of Colonies/plate		549	525	205	608	355
[Positive control with S9mix]						
Chemical		2AA	2AA	2AA	2AA	2AA
Dose(ug/plate)		1	2	10	0.5	2
Mean number of Colonies/plate		1061	450	811	536	442

AF2: 2-(2-Furyl)-3-(5-nitro-2-furyl)acrylamide, SA: Sodium azide, 9AA: 9-Aminoacridine, 2AA: 2-Aminoanthracene
*: Growth inhibition was observed.

Table 2.Mutagenicity of OCBC on bacteria (2)

With or without S9mix	Test substance dose (ug/plate)	Mean number of revertant colonies/plate: Base-pair substitution type			Frameshift type	
		TA 100	TA 1535	WP2 urvA	TA 98	TA 1537
without (-)	0	146	10	22	26	10
	15.6	168	11	20	18	8
	31.3	171	9	26	19	6
	62.5	202	11	25	26	13
	125	227	14	27	23	10
	250	25*	0*	5*	0*	1*
	500	0*	0*	0*	0*	0*
	0	138	14	27	33	12

	15.6	151	11	30	34	13
with	31.3	153	11	29	31	13
(+)	62.5	157	9	28	28	13
	125	187	11	35	32	10
	250	109*	6*	32	24*	7*
	500	0*	0*	0*	0*	0*
[Positive control without S9mix]						
Chemical		AF2	SA	AF2	AF2	9AA
Dose(ug/plate)		0.01	0.5	0.01	0.1	80
Mean number of Colonies/plate		543	562	201	588	471
[Positive control with S9mix]						
Chemical		2AA	2AA	2AA	2AA	2AA
Dose(ug/plate)		1	2	10	0.5	2
Mean number of Colonies/plate		1031	404	732	473	337

AF2: 2-(2-Furyl)-3-(5-nitro-2-furyl)acrylamide, SA: Sodium azide, 9AA: 9-Aminoacridine, 2AA: 2-Aminoanthracene
*: Growth inhibition was observed.

Table 3.Mutagenicity of OCBC on bacteria (3)

With or without S9mix	Test substance dose (ug/plate)	Mean number of revertant colonies/plate — Base-pair substitution type		
		TA100a	TA100b	TA100c
	0	131	149	132
	90	235	194	195
without	120	276	240	237
(-)	150	258	265	224
	180	136*	143*	142*
	210	0*	0*	16*
	240	0*	0*	0*
[Positive control without S9mix]				
Chemical		AF2	AF2	AF2
Dose(ug/plate)		0.01	0.01	0.01
Mean number of Colonies/plate		503	522	495

AF2: 2-(2-Furyl)-3-(5-nitro-2-furyl)acrylamide
*: Growth inhibition was observed.
a: Additional test 1, b: Additional test 2, c: Confirmation test

Test condition: Triplicate plates were used for each of six different concentrations of the sample. The liver microsome fraction (S9) was prepared from the liver of Sprague-Dawley rats pretreated with phenobarbital and 5,6-benzoflavon. The result was considered positive if the number of colonies found was twice the number of colonies of the control, which was exposed to dimethylsulfoxide, the solvent for o-chlorobenzyl chloride (OCBC), and concentration-related increase over the range tested and reproducible increase at

one or more concentrations were observed.
Test substance: -Source: Ihara Chemical Industry Co., Ltd.-Lot No.T7030-Purity: 99.65%
Reliability: (1) valid without restriction
OECD Guideline study
Flag: Critical study for SIDS endpoint
25-NOV-2004 (30)

Type: Ames test
System of testing: Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538, Escherichia coli WP2 uvrA
Concentration: 0.8 - 1,500 ug/plate
Cytotoxic Concentration: Without metabolic activation: >= 1,500 ug/plate
with metabolic activation: >= 500 ug/plate
Metabolic activation: with and without
Result: negative

Method: other:Ames B. N. et al. 1973
Year: 1983
GLP: yes
Test substance: other TS:- Source: HOECHST AG

Remark: The method was in principle equivalent to OECD Guideline 471 except that no follow-up experiments were done for confirmation of negative results.
Result: The number of revertant colonies did not increase compare with the solvent control in S. typhimurium , and E. coli WP2 uvrA, both with and without metabolic activation.

Table 1

With or without S9mix	Test substance dose (ug/plate)	Mean number of revertant colonies/plate					
		Base-pair substitution type			Frameshift type		
		TA 100	TA 1535	WP2 urvA	TA 98	TA 1537	TA 1538
without (-)	0	154	12	30	25	12	10
	0.8	169	15	26	22	12	12
	4	159	13	26	22	14	11
	20	152	12	29	19	13	8
	100	186	13	28	14	0.5	9
	500	*	*	13	*	*	*
	1,500	**	**	*	**	**	**
with (+)	0	163	16	49	30	15	19
	0.8	158	11	52	29	15	16
	4	151	15	44	32	15	19
	20	175	14	44	32	14	16
	100	188	11	44	23	13	15
	500	123	6	27	18	6	12
	1,500	*	**	19	7	*	*

[Positive control without S9mix]

Chemical	MD	SC	ENNG	MD	9AA	MD
Dose(ug/plate)	5	5	2	5	100	5

Mean number of Colonies/plate	3405	>5000	633	3170	>5000	3035	
[Positive control with S9mix]							
Chemical	2AA	2AA	2AA	2AA	2AA	2AA	
Dose(ug/plate)	0.5	1	10	0.5	1	0.5	
Mean number of Colonies/plate	715	156	2330	750	136	740	

MD: Methylhydrazone Derivative, SC: Streptocotocine,
ENNG: N-Ethyl-N-nitro-N-nitrosoguanidine,
9AA: 9-Aminoacridine, 2AA: 2-Aminoanthracene
*: no colony growth, **: no bacterial growth

These results have led to the conclusion that OCBC was not mutagenic under the conditions of this study.

Test condition: Quadruplicate plates were used for each of six different concentrations of the sample and for the solvent control. The liver microsome fraction (S9) was prepared from the liver of Sprague-Dawley rats pretreated with Aroclor 1254R (polychlorinated biphenyl). The result was considered positive if the number of colonies found was twice the number of colonies of the control, which was exposed to dimethylsulfoxide, the solvent for the substance in test, and concentration-related increase over the range tested.

Reliability: (2) valid with restrictions
Comparable to guideline study with acceptable restrictions

Flag: Critical study for SIDS endpoint

25-NOV-2004 (6)

Type: Chromosomal aberration test
System of testing: Chinese hamster lung (CHL/IU) cells
Concentration: 0.0013 - 0.02 mg/mL (without metabolic activation)0.013 - 0.2 mg/l (with metabolic activation)
Cytotoxic Concentration: without metabolic activation (continuous treatment): 0.010 mg/mL with metabolic activation (short-term treatment): 0.10 mg/mL
Metabolic activation: with and without
Result: positive

Method: OECD Guide-line 473
Year: 1999
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Result: Lowest concentration producing cytotoxic effects was 0.01 mg/mL without metabolic activation, and was 0.10 mg/mL with metabolic activation. Chromosome analysis was not performed at 0.02 mg/mL for continuous treatment and 0.20 mg/mL for short-term treatment. Cells with structural chromosomal aberrations, including gaps were increased at 0.10 mg/mL after short-term treatment with metabolic activation (frequency: 13.0 %). Polyploidy was induced at 0.10 mg/mL after short-term treatment with metabolic activation (frequency: 2.88%) and at 0.010 mg/mL after continuous treatment for 24 h (frequency: 3.38%).

Table 1.Cytotoxicity in Chinese hamster cells continuously treated with OCBC without S9 mix.

Time (hr)	Conc. (mg/ml)	Total no of cells		% of control
		dish 1	dish 2	
24	0	7438	8304	100.0
	0.0013	8934	8202	108.9
	0.0025	8751	8624	110.4
	0.0050	8674	8254	107.5
	0.010	6466	5679	77.1
	0.020	2629	1830	28.3
48	0	12622	12117	100.0
	0.0013	11499	9287	84.0
	0.0025	9900	8780	75.5
	0.0050	11819	9526	86.3
	0.010	8544	9855	74.4
	0.020	1717	1071	11.3

Table 2.Cytotoxicity in Chinese hamster cells treated with OCBC for 6 hr with or without S9 mix.

Conc. (mg/ml)	Total no of cells		% of control
	dish 1	dish 2	
[without S9 mix]			
0	5766	5796	100.0
0.0013	5068	5760	93.6
0.0025	6619	5571	105.4
0.0050	5829	5722	99.9
0.010	4951	5155	87.4
0.020	2303	2728	43.5
[with S9 mix]			
0	6967	6128	100.0
0.013	6035	6229	93.7
0.025	5654	6022	89.2
0.050	6368	5966	94.2
0.10	5425	5752	85.4
0.20	354	293	4.9

Table 3.Chromosome analysis of Chinese hamster cells continuously treated with OCBC without S9 mix.

Conc. (mg/ml)	Time of exposure (hr)	No. cells analysed	Total no. of structural aberrations	TAG (%)	TA (%)	Polyploid (%)
0	24	200	1	1 (0.5)	1 (0.5)	0.00
0.0025	24	200	2	2 (1.0)	1 (0.5)	0.13
0.0050	24	200	1	1 (0.5)	1 (0.5)	0.38
0.010	24	200	10	7 (3.5)	6 (3.0)	3.38*
0.020**	24	-				
0	48	200	1	1 (0.5)	1 (0.5)	0.13
0.0025	48	200	3	3 (1.5)	2 (1.0)	0.00

0.0050	48	200	0	0 (0.0)	0 (0.0)	0.00
0.010	48	200	0	0 (0.0)	0 (0.0)	0.75
0.020**	48	-				

TAG: total no. of cells with aberrations,
TA: total no. of cells with aberrations except gap,
*: Significantly different from solvent control at p<0.01 by Fisher's exact probability test.,
**: Chromosome analysis was not performed because there was small number of metaphase due to cytotoxicity.

Table 4.Chromosome analysis of Chinese hamster cells treated with OCBC with and without S9 mix.

Conc. (mg/ml)	Time of exposure (hr)	No. cells analysed	Total no. of structural aberrations	TAG (%)	TA (%)	Polyploid (%)
[without S9 mix]						
0	6	200	0	0 (0.0)	0 (0.0)	0.00
0.0025	6	200	1	1 (0.5)	1 (0.5)	0.25
0.0050	6	200	0	0 (0.0)	0 (0.0)	0.38
0.010	6	200	1	1 (0.5)	1 (0.5)	0.50
0.020**	6	-				
[with S9 mix]						
0	6	200	0	0 (0.0)	0 (0.0)	0.13
0.025	6	200	0	0 (0.0)	0 (0.0)	0.00
0.050	6	200	4	4 (2.0)	4 (2.0)	0.50
0.10	6	200	34	26* (13.0)	25* (12.5)	2.88*
0.20**	6	-				

TAG: total no. of cells with aberrations,
TA: total no. of cells with aberrations except gap,
*: Significantly different from solvent control at p<0.01 by Fisher's exact probability test.,
**: Chromosome analysis was not performed because there was small number of metaphase due to cytotoxicity.

Test condition: Duplicate plates were used for each of five different concentrations of the sample (0.0013, 0.0025, 0.0050, 0.010 and 0.020 mg/mL for continuous treatment (24 and 48 hr) and short-term treatment (6 hr) without metabolic activation; 0.013, 0.025, 0.050, 0.10, 0.20 mg/mL for short-term treatment (6 hr) with metabolic activation). The co-factor-supplemented post-mitochondrial fraction (S9) was prepared from the livers of male SD rats treated with phenobarbital and 5,6-benzoflavon. Mytomycin C and cyclophosphamide were used for the positive control.
Test substance: - Source: Ihara Chemical Industry Co., Ltd.- Lot No.: T7030- Purity: 99.65%
Reliability: (1) valid without restriction
OECD Guideline study
Flag: Critical study for SIDS endpoint
25-NOV-2004 (29)

5.6 Genetic Toxicity 'in Vivo'

Type: Micronucleus assay
Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of admin.: gavage
Exposure period: Twice at an interval of 24 hours
Doses: 50, 150, 500 mg/kg bw
Result: negative

Method: OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year: 2003
GLP: yes
Test substance: other TS:-Source: Clariant GmbH-Batch No. DEBG 047131-Purity: 99.6%

Result: Oral administration of 500 mg/kg bw resulted in the death of one male out of 10 animals treated. This animal was replaced and survived after treatment. The following signs of toxicity were observed in the main study from 2 hours to 6 hours after the second application: diarrhea, stilted gait and cowering posture.

The dissection of the animals revealed no test substance related macroscopic findings.

Animals from the other dose groups (50 mg/kg bw, 150 mg/kg bw) showed neither clinical signs of toxicity nor macroscopic findings after dissection.

The bone marrow smears were examined for the occurrence of micronuclei in red blood cells. The results are summarized in Table 1.

The incidence of micronucleated polychromatic erythrocytes in the dose groups with o-chlorobenzyl chloride (OCBC) was within the normal range of the negative control groups (mean of micronucleated polychromatic erythrocytes per 2000 cells: 1.7-4.9). No statistically significant increase in micronucleated polychromatic erythrocytes was observed. The ratio of polychromatic erythrocytes to total erythrocytes in both male and female animals differed less than 20 % from the control value in all dose groups, but decreased dose dependently indicating slight toxicity in the highest dose group.

From the results, it was concluded that OCBC did not cause a substantial increase in micronucleated polychromatic erythrocytes and is not clastogenic in the micronucleus test in vivo under the conditions described in this study.

Table 1.Results

Sex	Dose (mg/kg bw)	Poly/ animal counted	Poly/ Ery Mean	Poly with MN Mean	Poly with MN Mean [%]
male	0-control	2000	0.47	3.0	0.15
male	50	2000	0.54	4.0	0.20
male	150	2000	0.51	3.2	0.16
male	500	2000	0.43	2.8	0.14

male	40-Endoxan	2000	0.46	30.8*	1.54
female	0-control	2000	0.49	3.0	0.15
female	50	2000	0.50	3.0	0.15
female	150	2000	0.50	3.2	0.16
female	500	2000	0.41	3.2	0.16
female	40-Endoxan	2000	0.40	22.8*	1.14

*= significantly different from control (p<0.05)

Test condition: The test substance was administered twice at an interval of 24 hours oral to the test animals at doses of 50, 150 and 500 mg/kg bw. The vehicle, sesame oil, was administered in the same way to the negative control groups. The study included a concurrent positive control using Endoxan R, which was administered once orally at a dose of 40 mg/kg bw. The animals were examined regularly for mortality and clinical signs of toxicity. Experimental design is summarized in table 2.

Table 2.Experimental design

Group	Dose (mg/kg bw)	Vol. (ml/kg bw)	Number of animals and sex	Killing time (hours p.a.)
1	0	10	5 males/5 females	24
2	50	10	5 males/5 females	24
3	150	10	5 males/5 females	24
4	500	10	5 males/5 females	24
5*	40	10	5 males/5 females	24
6**	500	10	3 males/3 females	24

*= positive control: Endoxan R containing cyclophosphamide, dissolved in distilled water
**= replacement group
hours p.a.= hours after administration

Reliability: (1) valid without restriction
OECD Guideline study

Flag: Critical study for SIDS endpoint

25-NOV-2004 (12)

5.7 Carcinogenicity

-

5.8.1 Toxicity to Fertility

Species: rat
Sex: male/female
Strain: Sprague-Dawley
Route of administration: gavage
Exposure Period: male: 14 days before mating and thereafter 31 days, female: 14 days before mating to day 3 of lactation
Frequency of treatment: daily
Premating Exposure Period
male: 14 days
female: 14 days
Duration of test: male: to day 45 female: to day 3 of lactation
Doses: 2, 10, 50 mg/kg/day

Control Group: other:yes, 0.1% Tween 80 solution was gavaged
NOAEL Parental: > 50 mg/kg bw
NOAEL F1 Offspring: > 50 mg/kg bw

Method: other:OECD Guideline 422, "Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test"
Year: 1999
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Result: Test substance had no effects in reproductive parameters such as the mating index, the fertility index, number of corpora lutea or implantations, the implantation index, the delivery index, the gestation index, gestation length, parturition or maternal behavior. On examination of neonates, there were no significant differences in number of offspring or live offspring, the sex ratio, the live birth index, the viability index or body weight. No abnormal findings related to the test substance were found for external features, clinical signs or necropsy of the offspring.
Test condition: Nine-week-old male and female rats were used. Twelve males and twelve females were used for each dose levels, 2, 10, and 50 mg/kg/day. Test substance was administrated by gavage. Males were dosed for 14 days before mating; during the mating period and up to the day before scheduled kill (total 45 days). Females were dosed for 14 days before mating, during the mating period, during the gestation and four days after delivery (total 41-48 days). For mating, one male to one female mating was used, and the female was placed with the same male until pregnancy occurs or 7 days have elapsed. Day 0 of pregnancy was defined as the day a vaginal plug or sperm was found. The rats were weighed at Day 3, 7 and 14, and weekly thereafter. During the gestation, females were weighed at Day 0, 7, 14 and 20 of gestation, and Day 0 and 4 of lactation. The body weights of the live pups were also recorded. Gestated females were delivered and lactated through Day4 of lactation. At the termination of the experiment, all rats were sacrificed and necropsied. All pups were also sacrificed and necropsied.
Test substance: -Source: Ihara Chemical Industry Co., Ltd.-Lot No.T7030-Purity: 99.65%
Reliability: (1) valid without restriction
OECD Guideline study
Flag: Critical study for SIDS endpoint
29-JAN-2004 (28)

5.8.2 Developmental Toxicity/Teratogenicity
-

5.8.3 Toxicity to Reproduction, Other Studies
-

5.9 Specific Investigations
-

5.10 Exposure Experience
-

5.11 Additional Remarks

Type: other:RESPIRATORY TRACT IRRITATION

Remark: Type:sensory irritation
Species:mouse, Swiss-Webster, male and female
Concentration:11.9, 24.2, 82.3 and 179.5 mg/m3
Exposure:vapour inhalation
Exposure time:30 min
Number of animals:4 animals per dose and sex, at least 4 doses
Result:RD50, male: 84.9 mg/m3. RD50, female: 69.4 mg/m3.
Method:Sensory irritation response was determined by measurement of respiratory rates using body plethysmography. Additionally inspiratory and expiratory airflow and tidal volume was measured.
Year:1993
GLP:not stated
Test substance:other TS- Source: Aldrich- Purity: >99%
Result:RD50, male: 85 mg/m3. RD50, female: 69 mg/m3. The potency for sensory irritation is defined as concentration necessary to reduce respiratory rate in mice by 50% (RD50). The exposure resulted in a characteristic change to the normal breathing pattern consisting of a lengthening of stage I of expiration.
Reliability: (2) valid with restrictions
Study report which meets basic scientific principles.
Flag: Critical study for SIDS endpoint

30-JAN-2004 (37)

Type: other:RESPIRATORY TRACT IRRITATION

Remark: Type:sensory irritation
Species:mouse, Swiss-Webster, male
Concentration:not stated
Exposure:vapour inhalation
Exposure time:10 min
Number of animals:4 animals per dose, at least 4 doses
Result:RD50: 4.9 ppm
Method:Sensory irritation response was determined by measurement of respiratory rates using body plethysmography.
Year:1992
GLP:not stated
Test substance:other TS- Source: Monsdanto Co.- Purity: 99%
Result:RD50: 4.9 ppm corresponding to about 32.9 mg/m3. The potency for sensory irritation is defined as concentration necessary to reduce respiratory rate in mice by 50% (RD50).
Reliability: (2) valid with restrictions
Study report which meets basic scientific principles.

29-JAN-2004 (13)

Type: other:RESPIRATORY TRACT IRRITATION

Remark: Type:sensory irritation
Species:mouse
Concentration:not stated
Exposure:vapour inhalation
Exposure time:not stated
Number of animals:not stated
Result:log RD50: 0.756 (ppm)
Method:not stated
Year:1998
GLP:not stated
Test substance:other TS
Result:log RD50: 0.756 corresponding to 5.7 ppm corresponding to about 38.3 mg/m3. The potency for sensory irritation is defined as concentration necessary to reduce respiratory rate in mice by 50% (RD50).
Remark:RD50-value was taken from a secondary database.

Reliability: (4) not assignable
Only secondary literature

29-JAN-2004 (1)

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Appendix 1 The parameters used in the fugacity calculation (Level Ⅲ).

o-Chlorobenzyl chloride

Physicochemical parameters used

Molecular weight		161.03	Measured
Melting point [deg C]		-50	Measured
Vapour pressure [Pa]		2.04E+01	Estimated
Water solubility [g/m^3]		100	Measured
log Kow		3.32	Measured
half life [h]	in air	103	Estimated
	in water	33	Measured
	in soil	240,000	Default
	in sediment	720,000	Default

Temp. [deg C]	25

Environmental parameters used

		Volume [m^3]	Depth [m]	Area [m^2]	Organic carbon [-]	Lipid content [-]	Density [kg/m^3]	Residence time [h]
Bulk air	Air	1.0E+13					1.2	100
	Particles	2.0E+03						
	Total	1.0E+13	1,000	1E+10				
Bulk water	Water	2.0E+10					1,000	1,000
	Particles	1.0E+06			0.04		1,500	
	Fish	2.0E+05				0.05	1,000	
	Total	2.0E+10	10	2E+09				
Bulk soil	Air	3.2E+08					1.2	
	Water	4.8E+08					1,000	
	Solid	8.0E+08			0.04		2,400	
	Total	1.6E+09	0.2	8E+09				
Bulk sediment	Water	8.0E+07					1,000	
	Solid	2.0E+07			0.06		2,400	50,000
	Total	1.0E+08	0.05	2E+09				

Intermedia Transport Parameters

	[m/h]		[m/h]
Air side air-water MTC	5	Soil air boundary layer MTC	5
Water side air water MTC	0.05	Sediment-water MTC	1E-04
Rain rate	1E-04	Sediment deposition	5E-07
Aerosol deposition	6E-10	Sediment resuspension	2E-07
Soil air phase diffusion MTC	0.02	Soil water runoff	5E-05

Soil water phase diffusion MTC	1E-05	Soil solid runoff	1E-08

Appendix 1 (continued) Result of the calculation of the theoretical distribution *o*-Chlorobenzyl chloride

Scenario 1

	Emission rate [kg/h]	Conc. [g/m^3]	Amount [kg]	Percent [%]	Transfomation rate [kg/h]	
					Reaction	Advection
Air	1,000	5.8.E-06	5.8.E+04	64.1	3.9E+02	5.8.E+02
Water	0	5.1.E-05	1.0.E+03	1.1	2.1E+01	1.0.E+00
Soil	0	2.0.E-02	3.2.E+04	34.6	9.1E-02	
Sediment		1.1.E-03	1.1.E+02	0.1	1.0E-04	2.2.E-03
		Total amount	9.1.E+04			

Scenario 2

	Emission rate [kg/h]	Conc. [g/m^3]	Amount [kg]	Percent [%]	Transfomation rate [kg/h]	
					reaction	Advection
Air	0	6.7.E-07	6.7.E+03	12.2	4.5.E+01	6.7.E+01
Water	1,000	2.0.E-03	4.0.E+04	73.5	8.5.E+02	4.0.E+01
Soil	0	2.3.E-03	3.6.E+03	6.6	1.0.E-02	
Sediment		4.3.E-02	4.3.E+03	7.7	4.1.E-03	8.5.E-02
		Total amount	5.5.E+04			

Scenario 3

	Emission rate [kg/h]	Conc. [g/m^3]	Amount [kg]	Percent [%]	Transfomation rate [kg/h]	
					Reaction	Advection
Air	0	4.7.E-06	4.7.E+04	0.2	3.2.E+02	4.7.E+02
Water	0	3.3.E-04	6.7.E+03	0.0	1.4.E+02	6.7.E+00
Soil	1,000	1.5.E+01	2.4.E+07	99.8	6.9.E+01	
Sediment		7.0.E-03	7.0.E+02	0.0	6.8.E-04	1.4.E-02
		Total amount	2.4.E+07			

Scenario 4

	Emission rate [kg/h]	Conc. [g/m^3]	Amount [kg]	Percent [%]	Transfomation rate [kg/h]	
					Reaction	Advection
Air	600	4.2.E-06	4.2.E+04	1.7	2.8.E+02	4.2.E+02
Water	300	6.7.E-04	1.3.E+04	0.5	2.8.E+02	1.3.E+01
Soil	100	1.5.E+00	2.4.E+06	97.7	6.9.E+00	
Sediment		1.4.E-02	1.4.E+03	0.1	1.4.E-03	2.8.E-02
		Total amount	2.5.E+06			