

要 旨

試験委託者
環境庁

表 題

5-エチリデン-2-ノルボルネンの藻類(*Selenastrum capricornutum*)に対する生長阻害試験

試験番号

92065

試験方法

本試験は、OECD化学品テストガイドライン No.201「藻類生長阻害試験」(1984年)に準拠して実施した。

- 1) 被験物質：5-エチリデン-2-ノルボルネン
- 2) 試験生物：*Selenastrum capricornutum* (ATCC 22662株)
- 3) 初期細胞濃度： 1×10^4 細胞/mL
- 4) 暴露期間：72時間
- 5) 培養方式：振とう培養 (100 rpm)
- 6) 試験濃度：33.4、19.6、11.6、6.80、4.00 mg/L(公比：1.7)、助剤対照区及び対照区
- 7) 連 数：1試験区に付き3連
- 8) 試験液量：1試験容器(1連)に付き100 mL
- 9) 試験水温： $23 \pm 2^\circ\text{C}$
- 10) 照 明：4,000～5,000 lux (連続照明)
- 11) 試験液中の被験物質の分析：高速液体クロマトグラフィー (HPLC)
(暴露開始時、暴露終了時)

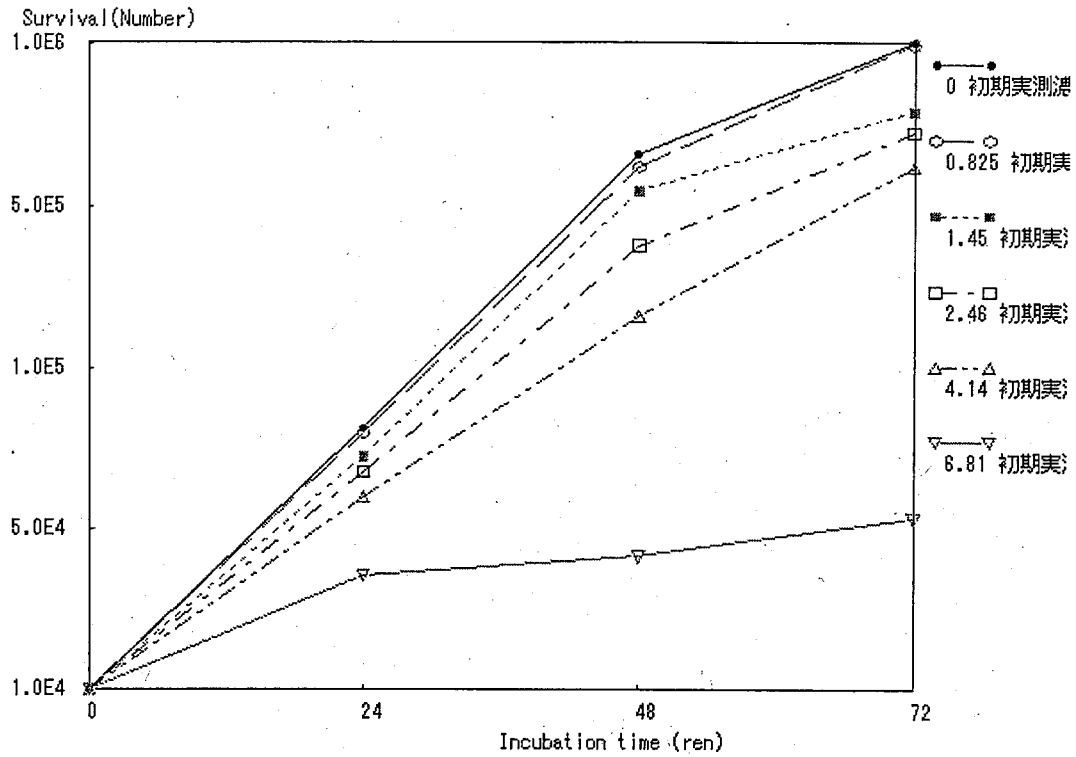
結 果

- 1) 生長曲線下の面積の比較による50%生長阻害濃度(E_0C50)及び最大無作用濃度(NOEC)
 $E_0C50(0-72h) = 2.61 \text{ mg/L}$ (95%信頼限界：2.15 ～ 3.18 mg/L)
 NOEC = 0.852 mg/L
- 2) 生長速度の比較による50%生長阻害濃度(E_0C50)及び最大無作用濃度(NOEC)
 $E_0C50(24-48h) = 4.28 \text{ mg/L}$
 NOEC = 1.45 mg/L
 $E_0C50(24-72h) = 5.31 \text{ mg/L}$
 NOEC = 0.852 mg/L

(上記濃度は、全て測定濃度に基づく)

5-エチリデン-2-ノルボルネン (CAS. 16219-75-3)

① 生長曲線



Time course pattern of Algae Growth Test
16219753初期実測濃度

② 毒性値

0-72hErC50(初期実測値に基づく)=4.9mg/L
0-72hNOECr(初期実測値に基づく)=0.78mg/L

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5-エチリデン-2-ノルボルネンのオオミジンコ(*Daphnia magna*)に対する急性遊泳阻害試験

試験番号

92066

試験方法

本試験は、OECD化学品テストガイドライン No.202「ミジンコ類、急性遊泳阻害試験及び繁殖試験」(1984年)に準拠して実施した。

- 1) 被験物質：5-エチリデン-2-ノルボルネン
- 2) 試験生物：オオミジンコ(*Daphnia magna*)
- 3) 生物数：20頭/試験区(1連につき5頭で1試験区20頭)
- 4) 暴露期間：48時間
- 5) 暴露方式：止水式(ガラス製板を用いた密閉式)
- 6) 試験濃度：5.00、2.78、1.54、0.857、0.476 mg/L(公比：1.8)、助剤対照区及び対照区
- 7) 連 数：1試験区につき4連
- 8) 試験液量：1試験容器(1連)につき約250 mL
- 9) 試験水温：20±1℃
- 10) 照 明：室内光、16時間明/8時間暗
- 11) 試験液中の被験物質の分析：高速液体クロマトグラフィー(HPLC)
(暴露開始時、暴露終了時)

結 果

- 1) 24時間暴露後の結果
24時間半数遊泳阻害濃度(EiC50)=3.34 mg/L (95%信頼限界：2.78～5.00 mg/L)
- 2) 48時間暴露後の結果
48時間半数遊泳阻害濃度(EiC50)=3.34 mg/L (95%信頼限界：2.78～5.00 mg/L)
最大無作用濃度(NOECi)=1.54 mg/L
100%阻害最低濃度=5.00 mg/L

(上記濃度は、全て設定濃度に基づく)

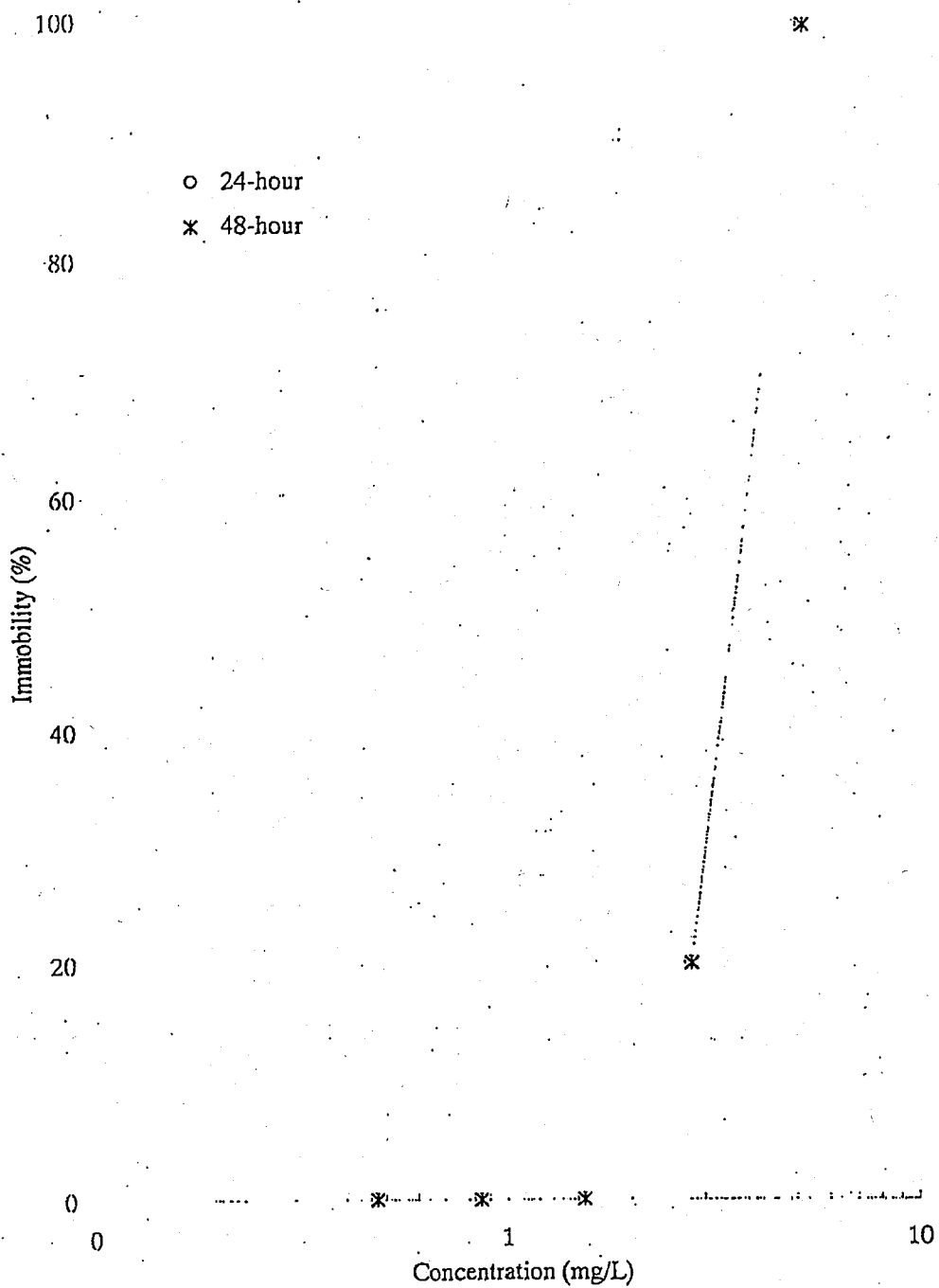


Figure 1. Concentration - toxicity curve of 5-ethylidene-2-norbornene in *Daphnia mc*

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表 題5-エチリデン-2-ノルボルネンのオオミジンコ(*Daphnia magna*)に対する繁殖阻害試験試験番号

92067

試験方法

本試験は、OECD化学品テストガイドライン No.202「ミジンコ類、急性遊泳阻害試験及び繁殖試験」(1984年4月採択)の改訂版であるガイドラインNo.211「オオミジンコ繁殖試験」(1997年4月提案)に準拠して実施した。

- 1) 被験物質：5-エチリデン-2-ノルボルネン
- 2) 試験生物：オオミジンコ(*Daphnia magna*)
- 3) 生物数：20頭/1試験区(1連につき5頭で1試験区20頭)
- 4) 暴露期間：21日間
- 5) 暴露方式：半止水式(毎日試験液を交換、ガラスシャーレを用いた密閉式)
- 6) 試験濃度：3.20、1.88、1.11、0.651及び0.383 mg/L(公比：1.7)、助剤対照区及び対照区
- 7) 連 数：1試験区につき4連
- 8) 試験液量：1試験容器(1連)につき約1300 mL
- 9) 試験水温：20±1℃
- 10) 照 明：16時間明(1,200 lux以下)/8時間暗
- 11) 試験液中の被験物質の分析：高速液体クロマトグラフィー (HPLC)
(0、1、7、8、14及び15日目)

結 果

- 1) 21日間の親ミジンコの50%致死濃度(LC50)
=2.57 mg/L
- 2) 21日間の50%繁殖阻害濃度(EC50)
=2.41 mg/L
- 3) 最大無作用濃度(NOEC)
=1.51 mg/L
- 4) 最小作用濃度(LOEC)
=2.57 mg/L

(上記濃度は、全て測定濃度に基づく)

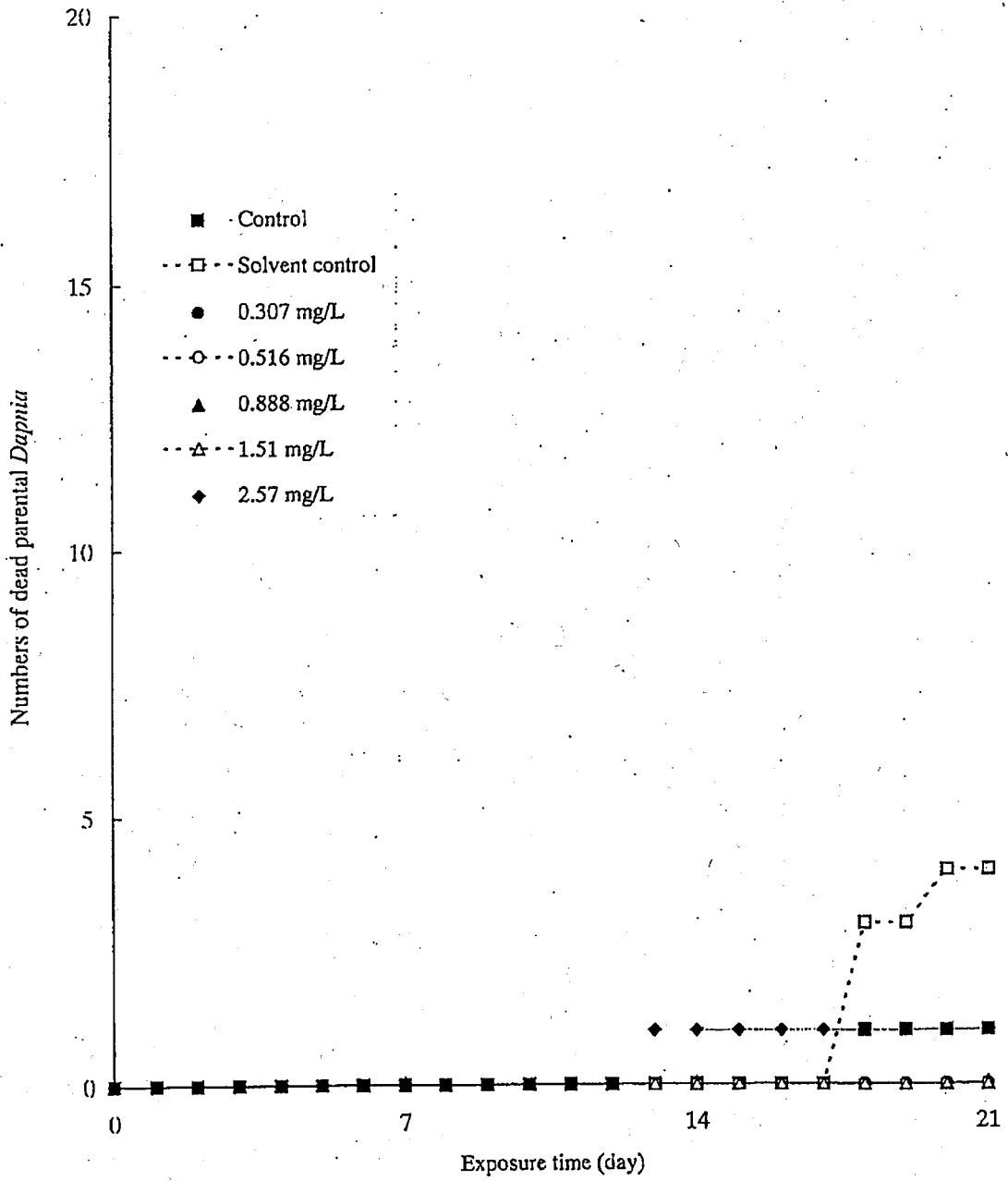


Figure 1. Cumulative numbers of dead parental *Daphnia*.

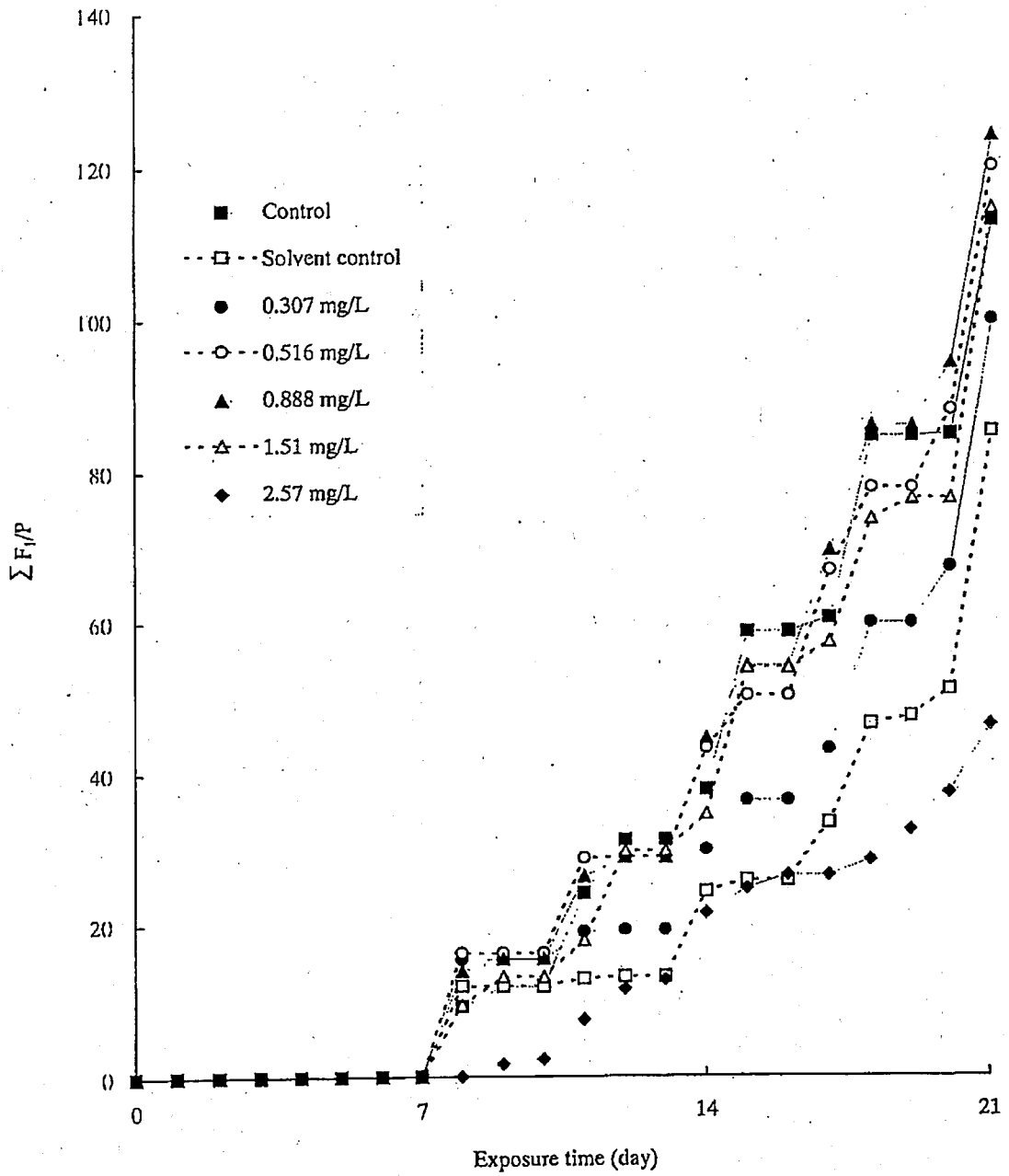


Figure 2. Mean cumulative numbers of juveniles produced per adult ($\Sigma F_1/P$).

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5-エチリデン-2-ノルボルネンのヒメダカ(*Oryzias latipes*)に対する急性毒性試験

試験番号

92068

試験方法

本試験は、OECD化学品テストガイドライン No.203「魚類急性毒性試験」(1992年)に準拠して実施した。

- 1) 被験物質：5-エチリデン-2-ノルボルネン
- 2) 試験生物：ヒメダカ(*Oryzias latipes*)
- 3) 生物数：10尾/1試験区(1連につき5尾で1試験区10尾)
- 4) 暴露期間：96時間
- 5) 暴露方式：半止水、密閉式(試験液調製後16時間目と8時間目に試験液を交換)
- 6) 試験濃度：20.0、14.3、10.2、7.29、5.21 mg/L(公比：1.4)、助剤対照区及び対照区
- 7) 連数：1試験区につき2連
- 8) 試験液量：1試験容器(1連)につき3.4 L
- 9) 試験水温：24±1℃
- 10) 照 明：室内光、16時間明/8時間暗
- 11) エアレーション：なし
- 12) 試験液中の被験物質の分析：高速液体クロマトグラフィー(HPLC)
[試験液調製時(暴露開始時、16時間後)、換水前(16時間後、24時間後)]

結 果

- 1) 96時間の半数致死濃度(LC50) = 7.00 mg/L (95%信頼限界：6.17~8.51 mg/L)
- 2) 0%死亡最高濃度 = 4.41 mg/L
- 3) 100%死亡最低濃度 = 8.51 mg/L
(上記濃度は、全て測定濃度に基づく)

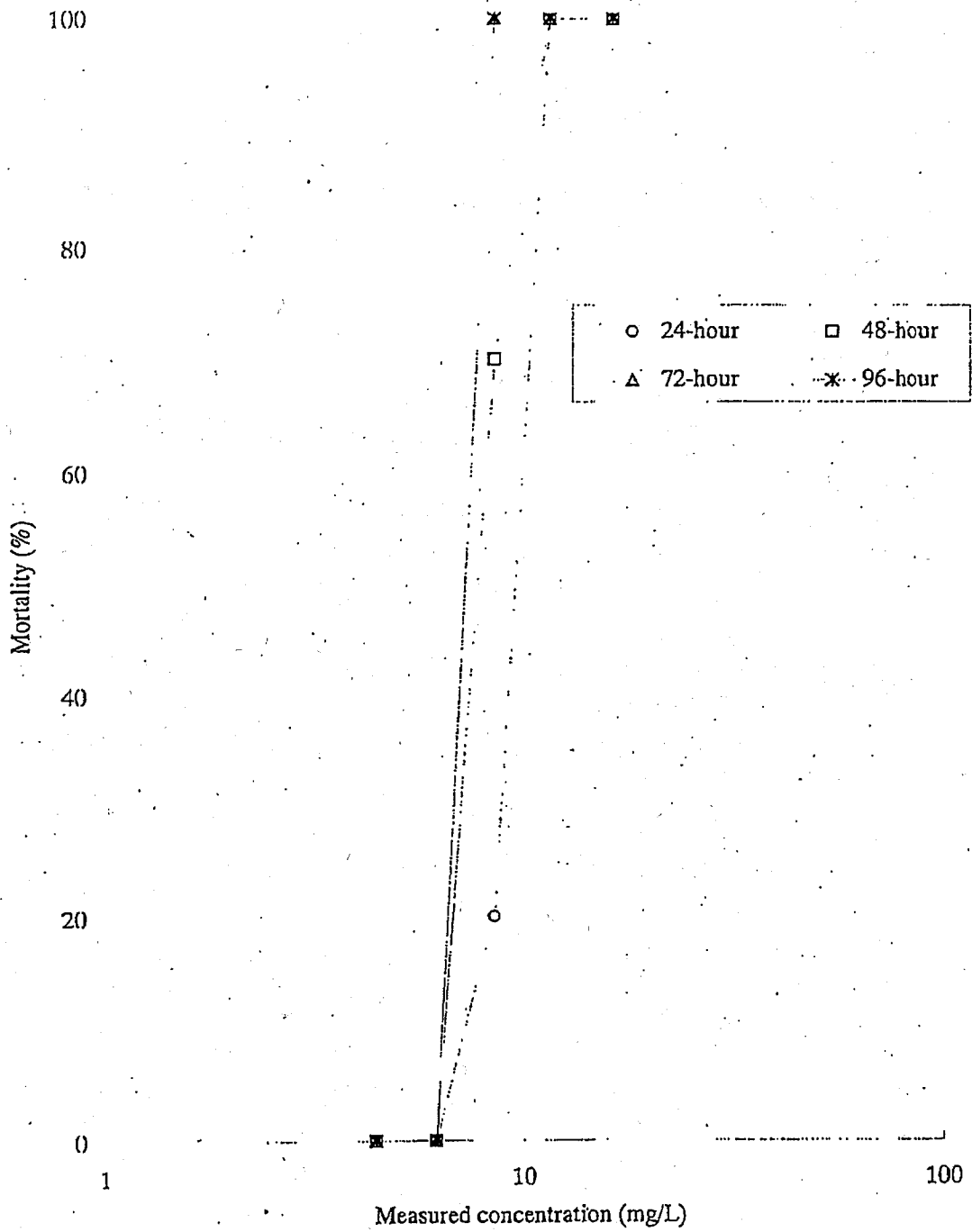
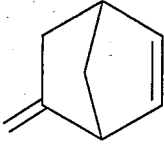


Figure 1. Concentration - toxicity curve of 5-ethylidene-2-norbornene in orange killifish (*Oryzias latipes*).

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	16219-75-3
Chemical Name	5-Ethylidene-2-norbornene
Structural Formula	 <chem>H3C=CHC12CC=CC1C2</chem>

RECOMMENDATIONS

The chemical is currently of low priority for further work.

SUMMARY CONCLUSIONS OF THE SIAR**Human Health**

Ethylidene norbornene (ENB) has a relatively low degree of acute toxicity in several species via oral (LD₅₀: 2276-5071 mg/kg), dermal (LD₅₀: >7168 mg/kg), and inhalation (LC₅₀: 13.3-14.8 mg/L or 2717-3015 ppm) routes of administration. The substance is a mild irritant to skin and is a slight eye irritant to rabbits. There are no data available on skin sensitization. Repeated dose toxicity data include one 28-d oral (gavage) study and 3 subchronic inhalation studies up to 14-wk in duration. In the 28-d repeated oral dose study [TG 407], relative kidney weights were increased in rats of both sexes given 100 mg/kg/d. Histopathological examination revealed increased hyaline droplets in proximal tubular epithelium of the kidney, and hypertrophy of follicular epithelium, as well as a decrease in colloid or irregularly shaped follicles in the thyroids of males given 4 mg/kg/d or more ENB. Hypertrophy of thyroid follicular epithelium and a decrease in colloid were also observed in females given 100 mg/kg/d. The LOAEL of ENB in the 28-d repeated dose study was reported as 4 mg/kg/d for males, and the NOAEL was 20 mg/kg/d for females. Because the male rat kidney effects are consistent with alpha-2u-globulin nephropathy they are not relevant to humans. The mechanism producing thyroid effects in rats has little or no relevance to humans. Therefore, the oral NOAEL for systemic effects other than thyroid and kidney is 20 mg/kg/d, based on reduced body weight of females in the 100 mg/kg group. In inhalation exposure studies in rats, the major toxicity also appeared in the thyroid. For the most recent rat study, the NOAEL was reported to be 5 ppm based on thyroid effects. Other than the thyroid, no exposure related lesions were observed at concentrations up to 149 ppm. Because the increased relative liver weights were seen in both sexes at 149 ppm, the inhalation NOAEL based on effects other than thyroid is considered to be 25 ppm. ENB was not mutagenic with and without an exogenous metabolic activation system in bacteria and mammalian cells *in vitro* [OECD TG 471, 472, 473]. The chemical induced neither chromosomal aberrations nor sister chromatid exchanges in mammalian cells in culture. It also did not induce dominant lethal mutation in rats. There are two key studies that evaluated reproductive and developmental toxicity. One is an oral reproductive / developmental toxicity screening test [OECD TG 421], and the other is an inhalation development toxicity (teratogenicity) study. In the OECD TG 421 study conducted in rats administered 0, 4, 20, and 100 mg/kg/day of ENB, a prolongation of the gestation period was noted in the 100 mg/kg/d group compared to controls but was within the normal historical range for the laboratory. The implantation and delivery indices were significantly lower in the 100 mg/kg/d group compared to controls. No other changes attributable to the compound were observed in any parameters including the mating index, the fertility index, the gestation index, number of corpora lutea, parturition state and lactation behavior. The total number of births and number of live offspring on

day 4 of lactation were decreased in the 100 mg/kg/d group. Among the pups, no other changes attributable to the compound were observed in parameters including the sex ratio, the live birth index, and the viability index on day 4, necropsy findings or external examination. Based on these findings, the oral NOAEL for reproductive/developmental toxicity was 20 mg/kg/d. A teratogenicity study was conducted in rats exposed by inhalation to 0, 25, 100 and 354 ppm ENB (0, 123, 492, 1740 mg/m³) during days 6-15 of pregnancy. There was no maternal mortality. Maternal body weights, body weight gain, and food consumption were reduced over the exposure period at 100 and 354 ppm, with partial or complete recovery post exposure. Increased relative liver weights were measured for the 100 and 354 ppm groups. There were no increases in the incidence of malformations or external and visceral variations. Three skeletal variants (bilobed 12th thoracic centrum, split 12th thoracic centrum, and poorly ossified second sternabra) were increased at 354 ppm, and one (bilobed 12th thoracic centrum) was increased at 100 ppm. Thus, fetotoxicity (skeletal variants) was seen in the 100 and 354 ppm group litters in the presence of maternal toxicity. For both maternal and developmental toxicity, 25 ppm (123 mg/m³) was a NOAEL.

Environment

ENB has been tested for aquatic toxicity in three trophic levels including fish, daphnia and algae. For acute toxicity, a 72hEC₅₀ of 2.61 mg/L and a 96hEC₅₀ of 3.68 mg/L for algae (OECD TG 201, *Selenastrum capricornutum* biomass), 48hEC₅₀ values of 3.34 and 7.3 mg/L for daphnid (OECD TG 202, *Daphnia magna*, immobilization), and for fish a 96hLC₅₀ of 7.0 mg/L (OECD TG 203, *Oryzias latipes*) and of 7.6 mg/L (*Brachydanio rerio*) were available. In chronic studies, a 72-h NOEC of 0.852 mg/L in *Selenastrum* (OECD TG 201, biomass) and a 21-d NOEC of 1.51 mg/L in *Daphnia magna* (OECD TG 211, reproduction) were reported, respectively. The EC₅₀ of multiple studies in different species of fish and in the daphnia and algae were consistent, however algae was the most sensitive among three trophic levels.

Exposure

The production volume of ENB is estimated to be ca. 20,000 tonnes/year in Japan, and ca. 54,000 tonnes/year worldwide; major producers are located in Japan, EU and the United States. ENB is a bicyclic diene compound used as a co-polymer in the production of ethylene-propylene diene monomer (EPDM) elastomers. ENB is produced in a closed system by a limited number of companies. At one company in Japan, ENB was not detected in the wastewater, rain sewer or in the air at the borderline of the Japanese manufacturing plant site. Data from one US manufacturer indicates 979 pounds (445 kg) per year are released as fugitive emissions to the atmosphere during production and storage of ENB. There are no discharges to soil or water (data reported to USEPA Toxic Release Inventory in 2000). The product use pattern can be described as "closed systems; non-dispersive use in the chemical industry as an intermediate." The major use of ENB is in EPDM rubber production, which occurs under controlled conditions. Data from a US and European EPDM plant have been obtained, and McKay Level III fugacity calculations indicate "nanogram" quantities of ENB will be present in water that enters the waste water treatment plant where most will be released to atmosphere prior to discharge. Based on physical/chemical properties [log Pow (3.82), water solubility (80 mg/L), vapor pressure (5.6 hPa), and Henry's Law constant (>5 atm·m³·mol⁻¹)] ENB released in the environment is readily volatile and will rapidly partition to the air (Fugacity level I calculations). ENB is not readily biodegradable (OECD 301C) and is expected to be slightly to moderately mobile in soil based on calculated soil adsorption coefficients (log K_{oc}) ranging from 2.96 to 3.01. Measured BCF of 61-160 in Carp confirm low potential for bioaccumulation (OECD 305C). If released into water, ENB is expected to volatilize to the atmosphere. The atmospheric half-life of ENB is estimated to be 52 minutes. Vapor phase ENB will be degraded in the atmosphere by reaction with photochemically produced hydroxy radicals and ozone molecules.

Occupational exposure to ENB may occur through inhalation and dermal contact with this substance at workplaces where ENB is produced and used. ACGIH and US/OSHA set a ceiling limit at 5 ppm (25 mg/m³) for ENB to protect against eye and skin irritation. Since ENB is produced in a closed system the potential for exposure is primarily during maintenance operations and/or upset conditions. Workplace air monitoring in the EPDM production area has found full shift personnel exposures normally below 0.5 ppm with a range of <0.01 to 1.39 ppm. In the rubber production areas, potential for worker exposures exist in and around the distribution conveyors to the baling pits. Short-term area samples from open points in the system vary from 1 to 5 ppm. The exposure to the general population via the environment is theoretically possible through consumption of fish, which may accumulate this chemical to a limited degree. However, due to the anticipated short residence time of ENB in aquatic ecosystems,

chronic exposure of aquatic organisms is not expected. Another possible exposure route may be via migration of the chemical from food packaging polymers. However, estimation of worst case exposures revealed very low exposure levels which were considered insignificant.

NATURE OF FURTHER WORK RECOMMENDED

The chemical is currently of low priority for further work This conclusion is based on negligible human exposure and very low environmental releases.