SIDS INITIAL ASSESSMENT PROFILE

| CAS No. | 88-09-5 |
|--------------------|--|
| Chemical Name | 2-Ethylbutyric acid |
| Structural Formula | HO CH ₃ CH ₃ |

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

The acid is primarily excreted unchanged in the urine as the glucuronic acid conjugate after oral and subcutaneous administration of 2-ethylbutyric acid in rabbits and rats. In dogs, 2-ethylbutyric acid undergoes β -oxidation and decarboxylation to yield 2-pentanone.

In an acute toxicity study of 2-ethylbutyric acid with rats, the oral LD_{50} was more than 2,000 mg/kg bw in both sexes. No acute inhalation or dermal studies are available for 2-ethylbutyric acid.

There are no experimental data on irritation and sensitisation.

In a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422), rats were given 2-ethylbutyric acid by gavage at 0, 10, 50, or 250 mg/kg bw/day. Males were dosed for a total of 42 days beginning 14 days before mating and females were dosed beginning 14 days before mating to day 4 of lactation throughout the mating and pregnancy period. There were no deaths related to this chemical. Transient salivation was observed in one male and one female at 250 mg/kg bw/day. There were no effects on body weight gain and food consumption in both sexes. In hematological examination, decreases in white blood cell count at 50 mg/kg bw/day and higher, and in platelet count were observed at 250 mg/kg bw/day in males, but no effects were found in females. There were no effects in blood chemistry and necropsy findings in both sexes. Increases in relative weight of the kidney in males and in absolute and relative weights of the kidney in females were noted at 250 mg/kg bw/day. In histopathological examinations, no toxicological changes were found in both sexes. Based on these findings, the NOAELs for repeated dose toxicity are considered to be 10 mg/kg bw/day in males and 50 mg/kg bw/day in females. There are no inhalation and dermal repeat dose studies available for 2-ethylbutyric acid.

This chemical was not mutagenic in anAmes test with and without exogenous metabolic activation, but this chemical was mutagenic in a chromosomal aberration test using CHL/IU cells without metabolic activation. In an *in vivo* mammalian erythrocyte micronucleus assay, no evidence of genotoxicity was noted. These data indicate that this chemical is not mutagenic *in vivo*.

There is no information available on carcinogenicity.

In the above mentioned combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422), histopathological examinations of the testes, epididymides and ovaries revealed no toxicological changes. No adverse effects were observed on reproductive parameters, such as estrous cycle, copulation index, fertility index, precoital interval, gestation length, numbers of corpora lutea and implantations, gestation index, implantation index and delivery index. Although poor maternal behavior or nursing was observed in three dams at 50 mg/kg bw/day and one dam at 250 mg/kg bw/day, no dose dependency was found. The number of live pups on days 0 and 4 of lactation, birth index and live birth index decreased at 250 mg/kg bw/day. There were no treatment-related changes in body weight, external appearance or necropsy findings in rat pups.

This document may only be reproduced integrally. The conclusions and recommendations (and their rationale) in this document are intended to be mutually supportive, and should be understood and interpreted together.

Based on these findings, the NOAEL for reproductive toxicity is considered to be 250 mg/kg bw/day (highest dose tested) and the NOAEL for developmental toxicity is considered to be 50 mg/kg bw/day.

Environment

2-Ethylbutyric acid is a colourless liquid with melting point of -31.8 °C, boiling point of 194 °C and vapour pressure of 0.08 mmHg at 20 °C (measured), 0.486 mmHg a5 25 °C (calculated). As 2-ethylbutyric acid is a weak acid with pKa of 4.69, this substance is expected to be dissociated in water in environmental conditions. This substance has a high water solubility of 17 g/L at 25 °C. The measured log Kow is 1.68 and and the calculated log Koc is 0.850. This substance is readily biodegradable under aerobic conditions. A calculated BCF value of 3.162 indicates that bioaccumulation in aquatic organisms is not expected. In the atmosphere, this substance is indirectly photodegraded by reaction with OH radicals with a half-life of 2.0 days. Environmental distribution using the Mackay level III model suggests that when 2-ethylbutyric acid is released into the environment, it distributes mainly into soil and water compartments (64.7 % in soil, 30.6 % in water, 4.55 % in air and 0.096 % in sediment).

Ecotoxicity data are available in aquatic species from three trophic levels. The GLP tests using a freshwater fish (OECD TG 203, *Oryzias latipes*), a daphnid (OECD TG 202, *Daphnia magna*) and green alga (OECD TG 201, *Pseudokirchneriella subcapitata*) were conducted. All toxicity tests were conducted without adjustment of pH although the test substance is acidic. Therefore organisms were subjected to both low pH effects and true toxic effects, if present, of the chemical.

The reliable acute aquatic toxicity results are:Oryzias latipes;96 h LC $_{50} > 50 \text{ mg/L}$ (<100 mg/L)</td>Daphnia magna;48 h LC $_{50} = 70 \text{ mg/L}$ Pseudokirchneriella subcapitata;72 h EC50 > 63 mg/L (rate method)Chronic toxicity results with daphnids (OECD TG 211, Daphnia magna) and algae (OECD TG 201,Pseudokirchneriella subcapitata) were available according to GLP tests. The reliable toxicity results are:Daphnia magna;21 d NOEC = 49 mg/LPseudokirchneriella subcapitata;72 h NOEC = 39 mg/L (rate and biomass method).

Exposure

The total production volume of 2-ethylbutyric acid was less than 500 tons/year in 2005 in the sponsor country. Information on the worldwide production volume is not available. In the sponsor country, 2-ethylbutyric acid is produced in a closed system for the main use as an intermediate. This substance is also used as a flavouring agent.

At production and processing sites, small amounts of 2-ethylbutyric acid might be released into waste-water stream. However, in the sponsor country, exposure of this substance into the environment should not be significant as the waste-water stream is treated with waste-water treatment plant and this substance is readily biodegradable.

2-Ethylbutyric acid is a semi-volatile liquid at normal temperature, and its $\log P_{ow}$ is 1.68, major occupational exposure routes are expected to be inhalation and dermal. Since the maximum vapour concentration is 247 ppm, exposure can be controlled by personal protective equipments even if workers are in direct contact with this chemical. Since this chemical is produced in a closed system and major use is as intermediates, direct contact is expected to be minimal. Workplace measurements data or occupational exposure limit values are not available. Even if consumer are exposed to this chemical, the level of exposure is expected to be very low, because this chemical is permitted only as a flavouring agent by Food Sanitation Law in the Sponsor country. This chemical can be used as a fragrance in cosmetics in other OECD countries.

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

Human Health: The chemical is currently of low priority for further work. The chemical possesses properties indicating a hazard for human health (repeated dose toxicity and developmental toxicity). Based on the data presented by the sponsor country (related to production by one producer in one OECD country which accounts

This document may only be reproduced integrally. The conclusions and recommendations (and their rationale) in this document are intended to be mutually supportive, and should be understood and interpreted together.

for an unknown fraction of the global production), exposure to humans is anticipated to be low. Countries may desire to investigate any exposure scenarios that were not presented by the sponsor country.

Environment: This chemical is currently of low priority for further work. The chemical possesses properties indicating a hazard for the environment (acute aquatic toxicity; LC_{50} values between 10 and 100 mg/l for algae, fish and daphnia). However, these hazards do not warrant further work because of the rapid biodegradation and limited potential for bioaccumulation of the chemical.

This document may only be reproduced integrally. The conclusions and recommendations (and their rationale) in this document are intended to be mutually supportive, and should be understood and interpreted together.