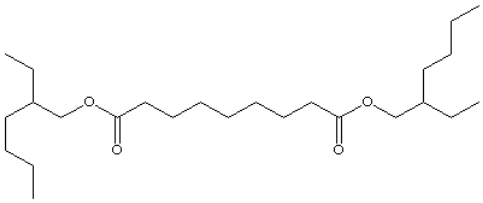
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	103-24-2
Chemical Name	Bis(2-ethylhexyl) azelate
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

There was no available information on toxicokinetics, metabolism and distribution.

In an acute toxicity study [OECD TG 401] of bis(2-ethylhexyl) azelate in rats, the oral LD_{50} was considered to be more than 2000 mg/kg bw in both sexes.

Available studies indicate that this chemical possessed low potential for skin and eye irritation. There was no available information on sensitisation.

In a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test [OECD TG 422], rats (13 animals/sex/dose) were given bis(2-ethylhexyl) azelate by gavage at 0, 100, 300 or 1000 mg/kg bw/day. Males were dosed for a total of 42 days beginning 14 days before mating and females were dosed for a total of 42-53 days beginning 14 days before mating to day 4 of lactation throughout the mating and pregnancy period. There were no deaths in any group. Body weight gain was suppressed in males at 1000 mg/kg bw/day. No changes in general conditions, food consumption, detailed clinical observations or neurobehavioral tests were found in males and females in any group treated with this chemical. Decreases in the number of white blood cells and levels of calcium were observed in females at 1000 mg/kg bw/day. The albumin/globulin (A/G) ratio was increased at 1000 mg/kg bw/day in both sexes and at 300 mg/kg bw/day in females. The increase in A/G ratio noted in females at 300 mg/kg bw/day was not considered as an adverse effect because no changes were observed in total protein or albumin at this dose. Lowered total protein was found in females at 1000 mg/kg bw/kg. Increases in relative weight of the liver in males and females, in absolute and relative weights of the kidney in males, and in relative weight of the kidney in females were noted at 1000 mg/kg bw/day. In histopathological examinations, a tendency of increased incidence of hypertrophy of the centrilobular hepatocytes was observed in males at 1000 mg/kg bw/day. Based on these findings, the NOAEL for repeated dose toxicity was considered to be 300 mg/kg bw/day in male and female rats.

This chemical was not genotoxic with or without an exogenous metabolic activation system in a bacterial test and in a chromosomal aberration test *in vitro*.

There was no available information 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. There were no adverse effects on copulation index, fertility index, precoital interval,

gestation length, gestation index or number of corpora lutea. No significant changes were observed in numbers of implantations and pups and live pups, and in indexes for implantation, delivery, birth and live birth. There were no treatment-related changes in body weight, external appearance or necropsy findings in offspring of rats. The NOAEL for reproductive and developmental toxicity was considered to be 1000 mg/kg bw/day.

Environment

Bis(2-ethylhexyl) azelate is a clear colourless liquid (melting point = -78 °C) without a specific odour. The substance has a very low vapour pressure (5.04 x 10^{-6} hPa at 25 °C) and water solubility (< 0.0004 mg/L at 20 °C). An experimentally obtained log Kow is 11.9 (by extrapolation) and a calculated log Koc (soil-adsorption co-efficient) is 5.48, and these parameters indicate that the water is not a target compartment. The substance is readily biodegradable under aerobic conditions (OECD TG301C, >94%, 28-d and 10-d window met). A calculated log BCF value of 0.5 indicates that bioaccumulation in aquatic organisms is not likely. Environmental distribution using Mackey level III suggests that when the substance is released into the environment, it distributes mainly into soil and sediment. In the atmosphere bis(2-ethylhexyl) azelate is indirectly photodegraded by reaction with OH radicals with a half-life of 0.4 days.

Eco-toxicity data of this chemical were 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 a green alga (OECD TG 201, *Pseudokirchneriella subcapitata*) were conducted as limit tests. No adverse effects were observed in the studies. The reliable acute aquatic toxicity results are:
Oryzias latipes; 96 h LC_{50} > 0.072 mg/L (> water solubility)
Daphnia magna; 48 h LC_{50} > 0.093 mg/L (> water solubility)
Pseudokirchneriella subcapitata; 72 h EC_{50} >0.08 mg/L (for both growth rate and biomass method, > water solubility)

Chronic toxicity results with daphnids (OECD TG 211, *Daphnia magna*) and algae (OECD TG 201, *Pseudokirchneriella subcapitata*) are available from GLP limit tests. These tests indicated that bis(2-ethylhexyl) azelate showed no adverse effects up to its water solubility. The reliable toxicity results are:
Daphnia magna; 21 d NOEC > 0.064 mg/L (> water solubility)
Pseudokirchneriella subcapitata; 72 h NOEC>0.08 mg/L (for both growth rate and biomass method, > water solubility).

Exposure

In Japan bis(2-ethylhexyl) azelate was commercially produced by at least four manufactures with an annual production volume of approximately ca. 150 tonnes in 2004. Worldwide production volume outside Japan was not available

Main use patterns (up to 95%) of bis(2-ethylhexyl) azelate produced and/or imported is used as a plasticizer for celluloses, polystyrene and vinyl plastics in order to improve low temperature resistance. A limited use of the substance as a lubricant at industrial sites was reported (less than 5%).

Bis(2-ethylhexyl) azelate is produced in a closed system and therefore significant exposure from the production and processing sites are not foreseen in the sponsor country. At production and processing sites, mainly during the maintenance and cleaning, bis(2-ethylhexyl) azelate can be released into wastewater streams and is treated by biological and chemical processes. During the use and due to deterioration of rubber products, it is expected that a small portion of the substance may be released into the environment. However, the substance is readily biodegradable and therefore exposure of the environment should not be significant.

Since the chemical has a very low vapour pressure and a low water solubility and high log Kow, exposure via inhalation route is unlikely and dermal uptake rate may be small, therefore exposure can be controlled by personal protective equipment in normal working conditions. At rubber production sites, where this chemical is used as plasticizer, mist may be released when rubber is treated at elevated temperature.
Although no quantitative data on the content of the substance in the final products is available, a trace level of consumer exposure through skin contact is expected.

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

This chemical is currently of low priority for further work because of its low hazard profile.