SIDS INITIAL ASSESSMENT PROFILE

CAS No.	___
Chemical Name	Primary Amyl Acetate-Mixed Isomers (commercial reaction process-derived mixture of approximately 65% 1-pentyl acetate (CAS No 628-63-7) and 35% 2-methyl-1-butyl acetate (CAS No 624-41-9))
Structural Formula	CH_3-CH_2-CH_2-CH_2-COO-CH_3 (1-pentyl acetate) CH_3-CH_2-CH(CH_3)-COO-CH_3 (2-methyl-1-butyl acetate)

SUMMARY CONCLUSIONS OF THE SIAR

Data are presented for Primary Amyl Acetate, which is the reaction process derived mixture of two isomers (1-pentyl acetate, CAS No 628-63-7 and 2-methyl-1-butyl acetate, CAS No 624-41-9) as well as individually for 1-pentyl acetate, the major component of Primary Amyl Acetate. Based on structural similarity with 1-pentyl acetate, toxicity data for 1-propyl acetate (CAS109-60-4) and 1-butyl acetate (123-86-4) were used to support the assessment of acute fish toxicity of Primary Amyl Acetate.

Human Health

Primary Amyl Acetate has an acute oral LD_{50} value of 12,306 mg/kg bw for female rats and >14,064 mg/kg bw for male rats. The dermal LD_{50} in male rabbits was 8359 mg/kg bw, and >14,080 mg/kg bw in females. Rats exposed for 6 hours to substantially saturated Primary Amyl Acetate vapor exhibited difficulty breathing; mortality was 20% among males exposed to 3693 ppm (19,646 mg/m^3) and 0% among females exposed to 3628 ppm (19,3000 mg/m^3). Primary Amyl Acetate causes moderate skin and eye irritation. Signs of respiratory irritation were noted in rats exposed to 3620 ppm (19,284 mg/m^3) Primary Amyl Acetate vapor. Human sensitization test data for Primary Amyl Acetate indicate that it does not induce dermal sensitization; negative results were also obtained in a human photoallergy test.

Information on repeated inhalation exposure is available in rats. Male and female rats were exposed by inhalation to 0, 100, 300, or 500 ppm (0, 532, 1596, 2660 mg/m^3) for 14 weeks displayed no clinical signs of toxicity and no mortality. All exposed males exhibited a very slight decrease in body weight gain relative to control males. The NOAEC for males and females was 500 ppm (2660 mg/m^3). In a 13-week inhalation neurotoxicity study, male and female rats were exposed to 0, 300, 600, or 1200 ppm (0, 1596, 3192, 6384 mg/m^3) Primary Amyl Acetate vapor. No mortality and no signs of toxicity were observed in any group. There were no neurobehavioral effects observed using motor activity measurements, functional observation battery testing, or neuropathological examinations. The NOAEC for neurotoxicity was 1200 ppm (6384 mg/m^3). There were no abnormalities observed in male and female rats fed Primary Amyl Acetate in their diet at concentrations of 0, 0.1, 0.5, or 1.0% for 90 days; doses in males were equivalent to 0, 68, 320, or 650 mg/kg bw/day; female doses were 0, 74, 350, and 720 mg/kg bw/day. The NOAEC for this study was 1% Primary Amyl Acetate in the diet, or based on the quantity of diet consumed, 650 and 720 mg/kg bw/day in males and females, respectively.

Primary Amyl Acetate has been tested *in vitro* in bacterial as well as animal cell cultures and is not genotoxic in these test systems both in the presence and absence of metabolic activation. Primary Amyl Acetate was negative when tested in a GLP chromosomal aberration assay in rat lymphocytes.

There were no significant effects observed on relative reproductive organ weights, and reproductive organs and tissues were normal in male and female rats exposed for 14 weeks to Primary Amyl Acetate vapor at concentrations up to 500 ppm (2660 mg/m^3). There were no effects observed on male and female reproductive organs and tissues in rats fed up to 1% Primary Amyl Acetate in the diet for 90 days.

In two developmental toxicity studies, pregnant female rats and rabbits were exposed to Primary Amyl Acetate vapor at concentrations of 0, 500, 1000, and 1500 ppm (0, 2660, 5320, 7980 mg/m^3) for 6 hours per day during organogenesis. Maternal toxicity was observed in rabbits at 1500 ppm (7980 mg/m^3) and in rats at all dose levels

as reduced food consumption and decreased maternal body weight gain. The decrease in corrected body weight gain during gestation in rats was significant at 1000 and 1500 ppm (5320 and 7980 mg/m^3). The NOAEC for maternal toxicity in rabbits and rats was 1000 and 500 ppm (5320 and 2660 mg/m^3), respectively. Among rabbits exposed between gestation day 6 and 18, no fetal malformations were observed and there was no evidence of developmental toxicity at any exposure level. Among rats exposed between gestation day 6 and 15, no fetal malformations were observed and overall incidence of variations was not increased. Female fetal body weights were reduced at 1000 and 1500 ppm. These fetal body weight decreases were accompanied by increases in one or three skeletal variations, at 1000 and 1500 ppm, respectively as well as two additional variations (one external and one visceral) at 1500 ppm. The NOAEC for developmental toxicity in rabbits and rats was 1500 and 500 ppm (5320 and 2660 mg/m^3), respectively.

Environment

The available physicochemical data are adequate to describe the properties of Primary Amyl Acetate. Primary Amyl Acetate has a vapour pressure of 5.73 hPa at 25ºC, and a water solubility of 1700 mg/L at 25 ºC. It has a boiling point of 146 ºC, a measured Log K_{ow} of 2.42, and an estimated melting point of -94ºC. The vapor pressure of its major component, 1-pentyl acetate, is 4.67 hPa at 25°C and its aqueous solubility is 2,000 mg/L at 20°C. The vapor pressure and aqueous solubility of the second component, 2-methyl butyl acetate were calculated by EPIWIN to be 8.46 hPa and 1,070 mg/L, respectively. The preferred log K_{ow} values of 1-pentyl acetate and 2-methyl butyl acetate are 2.34 and 2.26, respectively.

The photochemical removal of 1-pentyl acetate, as mediated by hydroxyl radicals, occurs with a calculated half-life of 34 to 43 hours. Photochemical removal of 2-methyl butyl acetate was calculated to be 41 hours. Primary amyl acetate is biodegradable under aerobic conditions. Primary Amyl Acetate is anticipated to volatilise easily from moving rivers, but only moderately from quiescent lakes and other surface water bodies; the calculated volatilisation half-life for Primary Amyl Acetate is between 3.4 hours from a river and 5.5 days (132 hours) from a lake. Primary Amyl Acetate is not likely to bioaccumulate in food webs. Based on Level III distribution modelling for 1-pentyl acetate, it is estimated that the majority of Primary Amyl Acetate released to the environment will partition into water (26.7%) and soil (66.3%), with a smaller amount in air (6.8%). The stability of primary amyl acetate in water is pH dependent. The predicted half-lives of Primary Amyl Acetate at 25 ºC at pH 4, 7, and 9 are 84.8, 138, and 21.9 days, respectively.

Primary Amyl Acetate exhibits low to moderate toxicity to fish, aquatic invertebrates and algae. Primary Amyl Acetate exhibited a 96-hr LC50 in fish of 69 mg/L. In *Daphnia magna*, the 48-hr EC50 was 40.9 mg/L. Finally, in green algae (*Pseudokirchneriella subcapitata*), Primary Amyl Acetate exhibited a 72-hr EC_r50 of >466 mg/L (growth rate) and a 72-hr EC_b50 (biomass) of 156 mg/L. Terrestrial data are not available for Primary Amyl Acetate or its components.

Exposure

Global production of Primary Amyl Acetate was estimated to be less than 10,000 tonnes in 2002. Consumption in 2002 was estimated to be 4,000 tonnes in the US, and 5,300 tonnes in Western Europe. In the United States, Primary Amyl Acetate is manufactured by one company in a continuous process in a closed system using engineering controls, which prevent the escape of liquid or vapors and minimizes release to the environment. Engineering controls are utilized during production, transfer, and loading operations to minimize exposure. The sole manufacturer of Primary Amyl Acetate in the U.S. does not isolate or market 1-pentyl acetate or 2-methyl-1-butyl acetate.

The predominant use of Primary Amyl Acetate is as a direct solvent component in the manufacture of OEM (original equipment manufacturers) factory-applied automotive paints and clearcoats. It is also used as a starting material and process solvent/extractant in the manufacture of pharmaceuticals. Primary Amyl Acetate may be present in cosmetics as a fragrance enhancer at ppm concentrations. The components of Primary Amyl Acetate have been identified in fruit and as naturally-occurring volatiles in cooked food.

Although its individual components may occur naturally in low concentrations in foods, Primary Amyl Acetate does not appear intentionally in food products, and is not approved as a direct or indirect food additive. It is a flammable liquid with a flammable range of 1.1 to 7.5 volume % in air (11,000 – 75,000 ppm) and a flash point of 37ºC (99ºF). The occupational exposure limit (ACGIH 8-hr TWA) for the components of Primary Amyl Acetate is 50 ppm.

The general population may be exposed to Primary Amyl Acetate as a fugitive emission. The individual components of Primary Amyl Acetate may also be released from food products, landfills, and sewage.

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

The following recommendations are applicable only to Primary Amyl Acetate-Mixed Isomers (reaction process-derived product) and not to its individual components.

Human Health: The product is currently a low priority for further work. The product possesses properties indicating a hazard for human health (skin, eye and respiratory tract irritation, and potential developmental toxicity). Based on data provided by the sponsor country (relating to production by one producer in the United States which account for an unknown fraction of the global production and relating to the use pattern primarily in the United States), risk management measures are being applied (engineering controls, occupational standards, Material Safety Data Sheets) in occupational settings. Countries may desire to check their own risk management measures for this product to find out whether there is need for additional measures.

Environment: The chemical has properties indicating a hazard for the environment (acute aquatic EC/LC50 values between 1 and 100 mg/l). However the product is of low priority for further work for the environment because of its rapid biodegradation and its limited potential for bioaccumulation.