# SIDS INITIAL ASSESSMENT PROFILE

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| **CAS No.** | ___ |
| **Chemical Name** | Primary Amyl Alcohol-Mixed Isomers (commercial reaction process-derived mixture of approximately 65% 1-pentyl alcohol (CAS No 71-41-0) and 35% 2-methyl-1-butyl alcohol (CAS No 137-32-6)) |
| **Structural Formula** | $CH_3$-$CH_2$-$CH_2$-$CH_2$-$CH_2$-OH (1-pentyl alcohol)<br>$CH_3$-$CH_2$-CH($CH_3$)-$CH_2$-OH (2-methyl-1-butyl alcohol) |

## SUMMARY CONCLUSIONS OF THE SIAR

### Analog Justification

Data are presented for Primary Amyl Alcohol, which is the reaction process derived mixture of two isomers (1-pentyl alcohol, CAS No 71-41-0 and 2-methyl-1-butyl alcohol, CAS No 137-32-6). Data from Primary Amyl Acetate toxicity studies have been included in the assessment of Primary Amyl Alcohol. Data from Primary Amyl Acetate are useful when assessing the hazards associated with the systemic toxicity of Primary Amyl Alcohol exposure due to the hydrolysis of Primary Amyl Acetate to Primary Amyl Alcohol *in vivo*. Exposure to Primary Amyl Acetate via inhalation exposure results in the appearance of Primary Amyl Alcohol in the systemic circulation. Since exposure to either Primary Amyl Acetate or Primary Amyl Alcohol results in systemic exposure to Primary Amyl Alcohol, systemic toxicity data from studies that administer Primary Amyl Acetate are useful in identifying hazards associated with Primary Amyl Alcohol exposure. Endpoints of Primary Amyl Alcohol toxicity that are associated with direct contact-mediated effects (e.g. eye, skin, and respiratory tract irritation) cannot be extrapolated from Primary Amyl Acetate data due to the difference in physical-chemical properties of the two materials. In addition, data from toxicity studies for 1-pentyl alcohol, the major component of Primary Amyl Alcohol, are included in the assessment for Primary Amyl Alcohol for human health endpoints.
Based on structural similarities and similar toxicities, data for 1-pentyl alcohol and 2-methyl butyl alcohol, the individual components of Primary Amyl Alcohol and for the 4-carbon structural analogs, 1-butyl alcohol (CAS No 71-36-6) and 2-methyl-1-propyl alcohol (CAS No 78-83-1) are also provided to address or augment environmental endpoints.

### Human Health

A recent *in vivo* respiratory bioavailability study confirmed the hydrolysis of Primary Amyl Acetate to Primary Amyl Alcohol. Blood levels of the alcohol isomers exceeded those of the acetate ester isomers at every time point tested, demonstrating the hydrolysis of the ester to the corresponding alcohols (1-pentyl alcohol and 2-methyl-1-butyl alcohol). These alcohols were then metabolized to their respective acids, resulting in increased systemic levels of 1-pentanoic acid and 2-methyl butyric acid. Thus, organisms exposed to Primary Amyl Acetate can experience appreciable tissue concentrations of Primary Amyl Alcohol. In this way, the results of toxicity studies with Primary Amyl Acetate can be used as supplemental, surrogate data to provide information on the toxicity of Primary Amyl Alcohol.

The acute oral $LD_{50}$ value for Primary Amyl Alcohol was 2690 mg/kg bw for male rats and 4989 mg/kg bw for female rats. The dermal $LD_{50}$ in female rabbits was 4110 mg/kg bw; erythema, desquamation, eschar, and necrosis were observed at the application site. There was 20% mortality among rats exposed to a saturated concentration of Primary Amyl Alcohol vapor (approximately 14,000 mg/m$^3$ or 3900 ppm) for 6 hours. Primary Amyl Alcohol is a corrosive liquid and causes severe skin and eye irritation. It should be considered a respiratory tract irritant. There are no animal or human sensitization test data for Primary Amyl Alcohol or its individual component isomers.

There are no repeated-dose studies available for Primary Amyl Alcohol. In a repeated inhalation exposure study, male and female rats were exposed by inhalation to Primary Amyl Acetate vapor at concentrations of 0, 100, 300, or 500 ppm (0, 532, 1596, or 2660 mg/m$^3$) for 14 weeks; rats displayed no clinical signs of toxicity and no mortality; the NOAEL for males and females was 500 ppm or 2660 mg/m$^3$. A 90-day repeated-dose oral toxicity

study is available for 1-pentyl alcohol, the major component of Primary Amyl Alcohol. Male and female rats received daily doses of 1-pentyl alcohol in corn oil by oral intubation at doses of 0, 50, 150, 500, or 1000 mg/kg bw/day for 13 weeks. There were no clinical signs of mortality and no lesions or abnormalities were observed. The NOAEL for this study for male and female rats was 1000 mg/kg bw/day.

Primary Amyl Alcohol has been tested *in vitro* in bacterial as well as animal cell cultures. The mixture was negative for mutagenicity in the presence and absence of metabolic activation in both the Ames assay and an HGPRT assay. Primary Amyl Alcohol did not induce an increase in chromosomal aberrations or in sister chromatid exchanges in mammalian cell assays conducted in the presence and absence of metabolic activation.

There are no reproductive toxicity studies available for Primary Amyl Alcohol. Data are available for Primary Amyl Acetate and 1-pentyl alcohol. 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 or 2660 mg/m$^3$. Similar results were obtained when male and female rats were exposed by oral gavage to 1-pentyl alcohol at doses up to 1000 mg/kg bw/day for 13 weeks.

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, or 7980 mg/m$^3$) for 6 hours per day during organogenesis. Maternal toxicity was observed in rabbits at 1500 ppm and in rats at all dose levels as reduced food consumption and decreased maternal body weight gain; the decrease in rats was significant at 1000 and 1500 ppm. The NOAEL 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 the 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 minor skeletal variations at 1000 and 1500 ppm, respectively, as well as external and visceral variations at 1500 ppm. The NOAEC for developmental toxicity in rabbits and rats was 1500 and 500 ppm (7980 and 2660 mg/m$^3$), respectively. Inhalation of 3900 ppm (14,040 mg/m$^3$) 1-pentyl alcohol vapor throughout gestation (day 1 through 19) produced maternal toxicity and a slight increase in the incidence of delayed ossification in rats, but no fetal malformations. These results suggest that Primary Amyl Alcohol may induce maternal and developmental toxicity at doses that induce maternal toxicity, but will not induce fetal malformations.

**Environment**

The available physicochemical data available for Primary Amyl Alcohol and its components are adequate to describe the properties of Primary Amyl Alcohol. Primary Amyl Alcohol has a vapor pressure of 3.3 hPa at 20ºC and a relative density of 0.816 g/cm$^3$; it has an estimated melting point of-110 ºC, a boiling point of 134.46ºC, and a log $K_{ow}$ of 1.42. The water solubility of Primary Amyl Alcohol is 23,200 mg/L at 25 ºC. Primary Amyl Alcohol is a flammable liquid with a flashpoint of 47ºC and a flammable range of 1.2 to 10.0 volume percent.
The physicochemical data available for the components of Primary Amyl Alcohol, 1-pentyl alcohol and 2-methyl butyl alcohol are also adequate to describe the properties of Primary Amyl Alcohol. 1-Pentyl alcohol and 2-methyl butyl alcohol have vapour pressures of 2.93 at 20 ºC and 3.4 hPa at 25ºC, respectively; the water solubility of 1-pentyl alcohol is 22,000 mg/L at 25ºC, the solubility of 2-methyl butyl alcohol is 30,000 mg/L at 25ºC; log $K_{ow}$ values for these two materials are 1.51 and 1.29, respectively.

The photochemical removal of 1-pentyl alcohol and 2-methyl butyl alcohol, as mediated by hydroxyl radicals, occurs with calculated half-lives of 30.9 and 29.93 hours, respectively. 1-Pentyl alcohol and 2-methyl butyl alcohol are readily biodegradable under aerobic conditions. Primary Amyl Alcohol volatilises moderately from moving rivers, but less so from quiescent lakes and other surface water bodies (calculated volatilisation half-lives of about 2 days from a river and 24 days from a lake). 1-Pentyl alcohol and 2-methyl butyl alcohol are not persistent in the environment and are not likely to bioaccumulate in food webs. Based on Level III distribution modelling, it is estimated that the majority of Primary Amyl Alcohol released to the environment will partition into water (36.8%) and soil (59.4%), with a smaller amount in air (3.7%).

Aquatic toxicity data are available for Primary Amyl Alcohol as well as its individual isomers, 1-pentyl alcohol and 2-methyl butyl alcohol. Static and flow through tests resulted in 96-hr $LC_{50}$s for fathead minnows between 472 and 606 mg/L. Since the duration of studies with *D. magna* (24 hours), green algae (8 days) and blue-green algae (8 days) with 1-pentyl alcohol is different than current OECD guidelines and because of uncertainties in study details, data for analogous compounds are presented. The analogous compounds used are 2-methyl-1-propyl alcohol and

1-butyl alcohol. For 2-methyl propyl alcohol, static tests were conducted using three water column-dwelling invertebrate species (*Daphnia magna*, *Daphnia pulex*, *Ceriodaphnia reticulata*) according to ASTM procedures. Forty-eight hour $EC_{50}$ values between 1100 and 1300 mg/L were reported for these species; for 1-butyl alcohol, a 48-hr $EC_{50}$ of 1328 mg/L was obtained for *Daphnia magna*. Using 1-butyl alcohol with the green algae *Pseudokirchneriella subcapitata* (formerly known as *Selenastrum capricornutum*), a 96-h $EC_{50}$ of 225 mg/L was reported. Terrestrial data are not available.

**Exposure**

Global production of Primary Amyl Alcohol was estimated to be approximately 35,000 tonnes in 1997. Consumption in 1997 was estimated to be 15,000 tonnes in the US, and 20,000 tonnes in Western Europe.

The predominant use of Primary Amyl Alcohol in the United States is as a chemical intermediate to provide the alkyl functionality in the lubricating oil additive, zinc diamyldithiophosphate (ZDDP or ZDDTP). Another major use is as an intermediate in the manufacture of Primary Amyl Acetate. Reported minor uses of Primary Amyl Alcohol are as a minor solvent in the manufacture of epoxy-based coatings, and nitrocellulose lacquers for factory-applied wood furniture finishes. It is also used in the manufacture of pharmaceuticals and xanthate ore floatation agents. A database search found no consumer products in the United States that contain Primary Amyl Alcohol. Both components of Primary Amyl Alcohol occur naturally in foods and may be released as plant volatiles. The major component of Primary Amyl Alcohol, 1-pentyl alcohol, is a direct food additive used as a synthetic flavoring agent. Although its individual components are present in very low concentrations in foods, Primary Amyl Alcohol is not approved for use as a direct or indirect food additive.

The occupational exposure limit for 1-pentyl alcohol, the major component of Primary Amyl Alcohol, is 100 ppm. Engineering controls are utilized during production, transfer, and loading operations to minimize flammability hazards and workplace exposure. Workplace exposure to Primary Amyl Alcohol during manufacture and use as industrial intermediate is anticipated to be limited in the US by an occupational exposure limit of 100 ppm.

Primary Amyl Alcohol may be released to the environment as a fugitive emission during production and use, or as naturally occurring emissions from food products, landfills, and sewage.

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

These recommendations are applicable only to Primary Amyl Alcohol-Mixed Isomers (reaction process-derived product) and not to its individual isomers.

**Human Health:** The product is currently of 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 a surrogate compound). Based on data provided by Sponsor country (relating to production by the sole manufacturer as well as two importers in the United States, which accounts 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 during manufacture (engineering controls, occupational standards, and Material Safety Data Sheets). Countries may desire to check their own risk management measures for this product to determine whether there is need for additional control measures.

**Environment:** The product is currently of low priority for further work due to its low hazard profile.