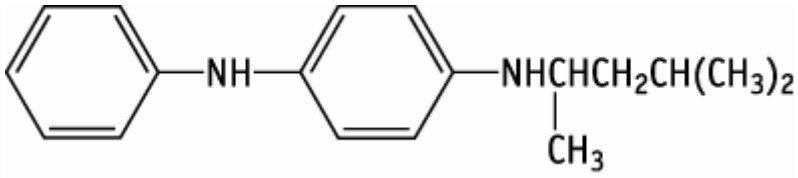
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	793-24-8
Chemical Name	N-(1,3-Dimethylbutyl)-N´-phenyl-1,4-phenylendiamine (6PPD)
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

No experimental data are available regarding the toxicokinetic behaviour and metabolism of 6PPD. The appearance of systemic toxicity after oral and dermal exposure shows the principal bioavailabilty of 6PPD via these routes.

The acute toxicity of 6PPD is moderate after oral administration and low after dermal application. The oral LD_{50} values in rats were 893 mg/kg bw for females and 1005 mg/kg bw for males. Signs of intoxication were hypoactivity, diarrhea, bradypnea, hypothermia and a prone position accompanied by pathological lesions in digestive organs and respiratory system. The dermal LD_{50} in rabbits was > 3000 mg/kg bw. Signs of intoxication were reduced food consumption, hypoactivity and lethargy.

The skin irritating potential of 6PPD is low. 6PPD is slightly irritating to the eye. The substance was found to induce dermal sensitization in experimental animals and humans. Positive patch-test results in humans partly may be related to para-group cross-sensitization.

The main targets identified after repeated oral intake of 6PPD by rats are the liver (increase of weight, fatty and vacuolar degeneration) and the blood cells (anemia, lymphocytopenia, and thrombocyto-sis). In studies with gavage covering exposure periods ranging from 28 to 48 days a NOAEL of 6 mg/kg bw/day and a LOAEL of 25 mg/kg bw/day can be derived based on a ca. 10 % increase in liver weight in both sexes as well as vacuolar liver degeneration in 2/12 males and salivation in males. From studies with exposure via the feed ranging from 13 weeks to 24 months a NOAEL of 75 mg/kg bw/day and a LOAEL of > 75 mg/kg bw/day can be derived both for male and female rats mainly based on anemia observed in the 13-week-study at a dose of 2500 ppm (ca. 150 mg/kg bw/day) which is higher than the top dose of 1000 ppm (ca. 75 mg/kg bw/day) tested in the chronic study. The higher NOAELs and LOAELs in feed studies are plausible taking into account the limited bioavailability of 6PPD when administered without lipophilic vehicle like corn oil used in the gavage studies.

In vitro 6PPD showed no mutagenic activity in bacterial and in mammalian cell test systems and it did not induce unscheduled DNA synthesis in primary rat hepatocytes. 6PPD showed clastogenic activity in CHL cells in vitro. 6PPD showed no clastogenic activity in the cytogenetic assay or the micro-nucleus test in vivo. Consequently the clastogenic activity reported in an in vitro test was not confirmed in vivo. In view of the clear negative finding in the in vivo test, there is no longer concern that 6PPD is likely to induce chromosomal aberrations in humans.

The underlying insufficiently documented studies with long-term application of 6PPD via diet gave no indication for a carcinogenic potential of 6PPD in rats.

In rats, up to oral doses of 100 mg/kg bw/day no impairment of reproductive performance was observed and there are no indications for teratogenic or developmental effects up to oral doses of 250 mg/kg bw/day (highest dose tested). Exposure during the gestation period demonstrated the absence of a developmental or teratogenic potential and of maternal toxicity in rabbits for doses up to 30 mg/kg bw/day (highest dose tested).

Environment

6PPD is a brown solid substance with a melting point of 50°C. 6PPD has a caluculated boiling point of 370 °C. It is nearly insoluble in water (1 mg/l at 20 °C). The vapour pressure was calculated to be 6.85×10^{-3} Pa at 25 °C. A log K_{ow} value of 4.68 was calculated. The flash point of the substance is 200 °C.

6PPD is not stable in water under environmental conditions. The half-life is less than 1 day under aerobic conditions. The major degradation products are 4-hydroxydiphenylamine, N-phenyl-p-benzoquinone monoimine and 1,3-dimethylbutylamine. The favourite target compartments of 6PPD are soil with 95 %, followed by water with 2 %, and sediment with 2 %, according to a Mackay calculation level I. The measured Henry's law constant of 1.84 $Pa*m^3*mol^{-1}$ indicates that the compound has a moderate potential for volatilization from surface waters. In the atmosphere rapid photodegradation takes place by reaction with photochemically produced OH radicals. The half-life is calculated to be 1 hour. On lighted surfaces and in the air, 6PPD will undergo direct photolysis due to absorbance of environmental UV light.

6PPD is not readily biodegradable but it is degraded rapidly in the environment. In an OECD TG 301C test on ready biodegradability, based on BOD, only ca. 2 % of 6PPD was biodegraded. Based on HPLC, ca. 92 % of 6PPD was removed within 28 d indicating that 6PPD was transformed. In another respirometer test according to OECD TG 301C 13 - 40 % of 6PPD were degraded within 28 d. In a River die-away test in Mississippi River water 6PPD was quantitatively removed (97 % within 22 h). The estimated half-lives are 2.9 h in biologically active river water, 3.9 h in sterile river water, and 6.8 h in sterile deionized water.

The calculated log K_{ow} indicates that 6PPD has a potential for bioaccumulation. 6PPD is not stable under certain environmental conditions. Bioaccumulation test results are available with some degradation products. Measured bioconcentration factors in Cyprinus carpio are in the range of < 1.2 - 23 for the degradation product N-phenyl-p-benzoquinone monoimine (concentration during incubation 6.83 µg/l or 0.683 µg/l), and in the range of < 1.7 - 17 for 1,3-dimethylbutylamine (concentration during incubation 0.2 mg/l or 0.02 mg/l). For 4-hydroxydiphenylamine a BCF of 30 was calculated. These data indicate that there is no potential for bioaccumulation of these metabolites.

In fish, the lowest acute toxicity was observed in *Oryzias latipes* during a test in accordance with OECD TG 203. A 96 h LC_{50} of 0.028 mg/l (effective concentration) was measured. In daphnids, the lowest effective LC_{50}/EC_{50} was a 48 h EC_{50} of 0.23 mg/l measured with *Daphnia magna* in a Guideline study according to OECD TG 202. In a "degradation toxicity" test with Daphnia magna, it was shown that 6PPD solution aged shortly (24 h) lost its toxicity towards *Daphnia magna*. Freshly prepared 6PPD solution exhibited a nominal 48 h NOEC of 0.25 mg/l and a 48 h LC_{50} of 0.51 mg/. Stirring for 24 h under areobic conditions at room temperature, decreased the toxicity of the test solution (containing 6PPD and degradation products) significantly. The 48 h NOEC of aged 6PPD was larger than 1 mg/l (highest exposure concentration). In a study according to the Algal Assay Procedure: Bottle Test of the US EPA with the green alga *Selenastrum capricornutum*, a 96 h $EC_{50}$of 0.6 mg/l (nominal) and a 96 h EC_{10} in the range of 0.2 mg/l were obtained.

It has to be considered that the toxicity observed in the reported studies was caused both by the 6PPD as well as by the degradation products due to the instability of the test substance.

Exposure

The total production of 6PPD is estimated to be about 130,000 t/a in 2001. 6PPD is used as rubber antidegradant which reacts as an excellent antiozonant. The main area of application is the rubber sector, with the majority of the manufacturing volume going into tyres.

Releases of 6PPD into the environment may occur from production, from use in the rubber industry and during use and disposal of rubber products.

In the Sponsor country, 6PPD is manufactured from 4-aminodiphenylamine (CAS No. 101-54-2) in closed systems. Manufacturing waste is incinerated.

6PPD is lost from rubber articles into the environment, due to tyre abrasion, evaporation from rubber surfaces, and losses from landfilled rubber wastes. There are no environmental monitoring data. Even in the vicinity of new tyres, no 6PPD was detected in the surrounding air.

In the manufacturing plant of the Sponsor company, workplace air sampling of precursors and auxiliaries, which are thought to be indicators of exposure, suggest that the exposure of workers to airborne 6PPD is negligible during manufacturing. In workplace areas of the rubber industry, most workplace concentrations were negligible (peak value of 6.6 mg/m^3). In workers of the Sponsor company no adducts with hemoglobin could be detected. 6PPD was found in 15 % of the urine samples (maximum was 1.3 µg/l urine) of 21 workers of the Italian rubber industry. In another study the concentration of 6PPD in urine samples of rubber industry workers was of < 1 to 300 µg/g creatinine (with a peak value of 580 µg/g) in 1982 to 1987.

RECOMMENDATION

The chemical is a candidate for further work

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health:

The chemical possesses properties indicating a hazard for human health (skin sensitization, anemia). It is therefore recommended that countries perform an exposure assessment, and, if then indicated, a risk assessment addressing exposure to workers and to humans via the environment.

Environment:

The chemical possesses properties indicating a hazard for the environment. Releases of 6PPD into the environment may occur during manufacturing in the rubber industry from the use of 6PPD as an antiozonant, as well as from the utilization of rubber products. Therefore, an exposure assessment and, if then indicated an environmental risk assessment is recommended. This should also include further investigations on identities and properties of degradation products.