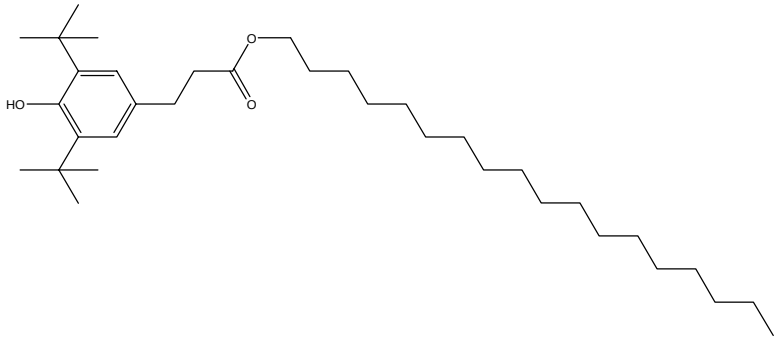
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	2082-79-3
Chemical Name	Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate can be taken up from the gastro-intestinal tract (23-35%) in the rat. After 168 hours 96% of the applied radioactivity was eliminated. No human data on toxicokinetics were available.

The acute oral LD_{50} of octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate in rats is >5000 mg/kg bw. Clinical signs included diarrhoea, sedation, dyspnoea, ruffled fur and hunched posture. For acute dermal toxicity the LD_{50} was >2000 mg/kg bw. Piloerection and hunched posture were noted. The LC50 for inhalation toxicity is >1811 mg/m^3 in the rat. Ruffled fur and ventral posture during exposure were reported. No human data on acute toxicity were available.

Based on tests with rabbits octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate was not considered to be a skin or eye irritant. No human data were available. No sensitization potential was found in the guinea-pig in a Maurer optimisation test. A human patch test confirmed this finding.

Repeated oral exposure to octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate induced effects on the liver (increased weight, hypertrophy), which were most probably related to induction of microsomal enzymes. No effect of duration of exposure and no species differences were observed in the oral studies available; a 28-day study in rats (mainly according to OECD TG 407, NOAEL 30 mg/kg bw/day, a 90-day study in dogs (NOAEL 32-37 mg/kg bw/day) and a 2-year study in rats (NOAEL 64-81 mg/kg bw/day). Therefore the NOAEL for oral toxicity was considered to be 30 mg/kg bw/day. For inhalation toxicity a NOAEL of 543 mg/m3 was derived (the highest concentration tested) from a 21-day study (6h/d; 5 d/wk).

Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl) propionate was negative in an Ames test and an *in vivo* micronucleus test. There were no indications that octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl) propionate possesses genotoxic properties.

In a 2-year dietary carcinogenicity assay in mice no increased tumour incidence was found at any of the dose levels tested (0, 0.6, 5.4 and 56 mg/kg bw/day).

In a two generation study in rats octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate (0, 500, 1500 and 5000 ppm) did not show any adverse effects on reproduction based on absence of effects on mating performance, pregnancy rate and gestation duration at 96-111 mg/kg bw/day (1500 ppm). The NOAEL for developmental

toxicity was 32-39 mg/kg bw/day (500 ppm) based on reduced growth and survival of the pups. In teratogenicity studies in rats and mice (0, 150, 500 and 1000 mg/kg bw/day mainly according to OECD TG 414) the NOAEL for maternal toxicity and teratogenicity was 1000 mg/kg bw/day. Decreased foetal weight (2-3% of control) and delayed ossification were reported at 500 and 1000 mg/kg bw/day in rats. These effects were considered not to be toxicologically relevant. Therefore the NOAEL for developmental toxicity was 1000 mg/kg bw.

Environment

Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl) propionate is a powder with a melting point of 49-54°C, calculated boiling point of 561°C and a calculated vapour pressure of 5.5E-07 hPa. The substance has a very low solubility in water (2.85 µg/l) and has a calculated log Kow of 13.4.

The substance is not readily biodegradable. However, 32-35% biodegradation was observed in a modified Sturm Test (OECD TG 301 B) over the 28 day study period (CO_2 evolution). In a modified MITI Test (OECD TG 301 C) 21-39% degradation was measured (BOD). Two metabolites were found and identified as 3-(3,5-di-tert-butyl-4-hydroxyphenyl) propionic acid and 1-octadecanol. The rate of the acid production amounts to 58-94%. The acid formed was not biodegraded. Although the substance contains an ester bond, hydrolysis is unlikely to be the main abiotic degradation process in waters. Hydrolysis half-live is estimated to be >7 years at pH 7 and 264 days at pH 8 (EPISUITE 3.12).

Calculations of the BCF with standard QSARs (EPISuite 3.12, EUSES 2.03) give a wide variation in results depending on the model selected (3 and 25 000). An experimental determination of the BCF is available indicating a low potential for bioaccumulation of the parent substance in fish. However the test was performed at a concentration in excess of the water solubility of the substance in presence of a dispersant. Therefore the available information does not allow concluding that the bioaccumulation is low. Bioaccumulation of degradation products is not assessed.

The calculated half-life for the photo-oxidation (reaction with hydroxyl radicals) of octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate in air is 3 hours (EPISuite 3.12). Level III fugacity modelling shows that after release to surface water 98% of the substance will partition to sediment. When released to soil 99.9% will remain in this compartment.

For octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl) propionate no effects at the water solubility level (2.85 µg/l) were observed in acute fish, daphnia and algae tests. Two static studies in fish according to OECD TG 203 showed no treatment related mortality. The 96-h LC50 for both species (*Lepomis macrochirus, Salmo gairdneri*) was >100 mg/l. *Daphnia magna* were exposed to the substance (dispersant used) during 24 hours in a static test (OECD TG 202). No effects on mobility were found at any of the concentrations tested (48-h EC50 is >100 mg/l). A 72h study with the algae *Scenedesmus subspicatus* showed no effect at the highest concentration tested (72-h E_rC50 >11.3 mg/l measured; growth rate).

Dry leaves were observed in turnip at 100 mg/kg dry soil weight in a test on seeds of ryegrass, turnip and vetch exposed to octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate at concentrations of 0, 1, 10 and 100 mg/kg dry soil weight.

Exposure

For the year 2004 the global market for octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl) propionate was estimated to be 50 000 tonnes. The primary use of the substance is as an antioxidant to prevent the deterioration of polymers. It acts as an inhibitor that reacts with O-centered radicals present in the substrate. Therefore the substance is degraded in complex reactions over the lifetime of the product to some extent.

Limited consumer exposure is expected from the primary use of octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl) propionate as phenolic antioxidant bound in a polymeric matrix (e.g. packaging materials). Minor uses of Octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl) are preparations such as adhesives, sealants, paints and lubricants (Swiss Product Register).

There is potential environmental exposure during production and processing of octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl) propionate and by leaching from waste in landfills.

Occupational exposure might occur during packaging and handling of the additive (e.g. opening of bags, blending or filling operations).

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

Human Health: The chemical is of low priority for further work due to its low hazard potential

Environment: Short-term aquatic toxicity tests at 3 trophic levels were available which show no effects at the water solubility level in any of the tests. However 3-(3,5-di-tert-butyl-4-hydroxyphenyl) propionic acid was found as a stable metabolite in a biodegradation study. Therefore the chemical is a candidate for further work. The aquatic hazard of this metabolite should be assessed. If distribution modelling of this metabolite shows that it will end up in the sediment, further testing of the toxicity on sediment dwelling organisms is recommended. Although apparent emissions of the parent substance at manufacturing and processing sites and emissions from the use of the substance in chemical preparations are expected to be low, a more detailed exposure assessment is necessary taking into account the acid formed during aerobic biodegradation of 3-(3,5-di-tert-butyl-4-hydroxyphenyl) propionate.