# SIDS INITIAL ASSESSMENT PROFILE

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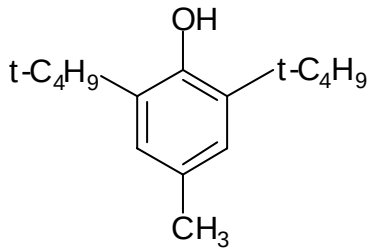
| **CAS No.** | 128-37-0 |
| **Chemical Name** | 2,6-di-tert.-butyl-p-cresol (BHT)<br>Butylated Hydroxytoluene |
| **Structural Formula** |  |



## RECOMMENDATIONS

The chemical is a candidate for further work.

## SUMMARY CONCLUSIONS OF THE SIAR

**Human Health**

BHT is of low acute toxicity. BHT caused acute toxic effects in mammalians but there were no specific clinical symptoms. In rats, the oral $LD_{50}$ was > 2930 mg/kg bw, the $LD_{50}$ after dermal exposure was > 2000 mg/kg bw. It was slightly irritating to the skin and eyes of rabbits.

On chronic oral exposure of rats, liver and thyroid are the main targets. Doses above 25 mg/kg bw/day BHT resulted in thyroid hyperactivity, enlargement of the liver, induction of several liver enzymes. 25 mg/kg bw/day BHT can be considered as NOAEL for chronic exposure. The haemorrhagic effects of high repeated doses of BHT seen in certain strains of mice and rats, but not in other species, may be related to its ability to interact with prothrombin and vitamin K.

BHT showed no potential to cause point mutations in several bacterial and mammalian *in vitro* test systems.

Overall, the available studies demonstrate that BHT has no clastogenic activity *in vitro* or *in vivo*. Most *in vitro* chromosome aberration assays were negative as were sister chromatid exchange assays and DNA damage and repair assays. *In vivo*, micronucleus assays with mice, cytogenetic assays with rats and mice, dominant lethal assays with rats and mice, and the heritable translocation assay with mice were also negative.

BHT is not a genotoxic carcinogen. Carcinogenic effects observed in one long-term study with rats probably were caused by the specific study conditions. However, it cannot be completely ruled out that the hepatotoxic effects caused by high and chronic doses of BHT may result in persistent cell proliferation, which is known as a possible mechanism of non-genotoxic carcinogens. In addition, depending on the application regime, BHT may exert either anticarcinogenic or tumour-promoting activity at relatively high doses. For the possible carcinogenic and tumour-promoting effect of BHT, a threshold level of 100 mg/kg bw/day can be assumed. At this dose, no increase in the incidence of liver carcinoma, but a slight increase in liver adenoma were observed after chronic exposure starting *in utero* as a worst case scenario.

The only effects on reproduction were lower numbers of litters of ten or more pups at birth at doses of 100 mg/kg bw/day and above. The NOAEL was 25 mg/kg bw/day.

From studies with mice and rats there is no evidence of teratogenic effects of BHT. During pregnancy BHT had maternal effects on mice above oral doses of 240 mg/kg bw/day. The NOEL for developmental toxicity was 800 mg/kg bw day.

Despite of being in wide dispersive use as ingredient of various products for many years only very few cases of allergic reaction in humans after dermal exposure or oral intake have been described. For the use of BHT as antioxidant in foodstuff an acceptable daily intake (ADI) of 0 - 0.3 mg/kg bw/day has been established.

**Environment**

BHT has a melting point of ca. 70 °C, a water solubility in the range of 0.6-1.1 mg/l (20-25 °C), a density of 1.03 g/cm³, and a vapor pressure of 1.1 Pa (20 °C). The measured log Kow is determined to be 5.1.

According to a Mackay Level I model calculation, the main target compartment for BHT is air (79-87 %), followed by soil (6.1-10.2 %) and sediment (5.7-9.5 %). Due to the instability of BHT in aqueous solution the estimations reflect a tendency for BHT distribution among environmental compartments. BHT is relatively unstable under environmental conditions. Extent and products of decomposition are dependent on several factors like irradiation, pH, temperature, moisture, presence of soil and soil microorganisms, and oxygen content. In air BHT is indirectly photodegradable by hydroxyl radicals with $t_{1/2}$ = 7.0 hours. In aqueous solution BHT is decomposed in natural sunlight with irradiation (ca. 75 %) and without (ca. 40 %), forming different, partly unidentified metabolites. BHT is also not stable in soil. Within one day of incubation 63-82 % of BHT were decomposed in non-sterilized and 25-35 % in sterilized soils. A mineralization up to 30 % was observed under non-sterilized conditions. Depending on the exposure pathways, the compartments air, hydrosphere and soil can be environmental target compartments for this substance and its metabolites. BHT is not readily biodegradable in water according to a modified MITI-I test (4.5 % degradation after 28 days). A wide range of bioconcentration factors (BCF) was found in different experiments. Bioconcentration factors (BCF) in the range of 230-2500 have been determined for fish after 56 days. The BCF values determined after a 28 days exposure period in a model ecosystem with soil were 2-17 for fish, 30 for snails and 38 for algae. It can be assumed that BHT has a moderate to high bioaccumulation potential in aquatic species.

For the toxicity of BHT on aquatic species reliable experimental results from tests with fish, daphnia, and algae are available. Only those effect values are considered for the assessment that did not exceed the low water solubility of BHT (0.6 - 1.1 mg/l) and were based on measured concentrations. The lowest reliable acute toxicity values are:

fish (*Brachydanio rerio*): 96h LC0 ≥ 0.57 mg/l;
invertebrates (*Daphnia magna*): 48h EC0 ≥ 0.17 mg/l;
algae (*Scenedesmus subspicatus*): 72h $E_rC_8$ = 0.4 mg/l. This value can be used as a NOEC.

In a 21 days reproduction test with *Daphnia magna* a NOEC = 0.07 mg/l was determined. Using an assessment factor of 50,a PNECaqua = 0.0014 mg/l is derived from this long term NOEC.

**Exposure**

In 2000, the world production capacity of BHT amounts to about 62,000 t/a by more than 20 producers. BHT is a registered antioxydant, licenced for food products, animal feed, cosmetics, and packaging material. It is also used in petroleum products, synthetic rubbers, plastics, elastomers, oils, waxes, soaps, paints, and inks.

Releases into the environment may occur during production of BHT as well as during its use in different applications as stabilizer and during the use of the products that contain the substance. A significant release into the environment is expected from migration of BHT onto the surface of products containing the substance.

## NATURE OF FURTHER WORK RECOMMENDED

**Environment**: The substance is a candidate for further work. Releases into the environment during use of BHT and from products containing the substance have to be assumed but are not quantifiable. In the environment, BHT is rapidly decomposed forming several, partly unidentified, metabolites. BHT is not readily biodegradable, a moderate to high bioaccumulation potential has to be assumed. The NOEC from the long-term toxicity to daphnids was 0.07 mg/l, resulting in a PNEC of 0.0014 mg/l. Therefore, the performance of an environmental risk assessment is recommended. Especially the questions concerning exposure, bioaccumulation as well as toxicity of the metabolites should be clarified.

**Human Health**: No recommendation for further work, because all SIDS endpoints are adequately covered and because exposure is controlled in occupational settings.