Butylated Hydroxytoluene  
(2,6-Bis(1,1-dimethylethyl)-4-methylphenol)

Butylated hydroxytoluene (BHT) is used as an antioxidant/preservative in foods at levels ranging from 10 to 200 ppm. Current food regulations establish a maximum content of 0.02 percent for all antioxidants combined. Industrial applications of BHT include use as an antioxidant in rubber, petroleum, and plastic products.

Butylated hydroxytoluene passed the animal data screen, underwent a preliminary toxicological evaluation, and is being brought to the Carcinogen Identification Committee for consultation. This is a compilation of the relevant studies identified during the preliminary toxicological evaluation.

**Epidemiological data**

No cancer epidemiology studies were identified.

**Animal carcinogenicity data**

- Long-term diet studies
  - 107 to 108-week diet studies in male and female B6C3F1 mice: NCI (1979)
    - Increase in alveolar/bronchiolar carcinomas or adenomas (by pairwise comparison) in females
    - No treatment-related tumor findings in males
  - 105-week diet studies in male and female Fischer 344 rats: NCI (1979)
    - No treatment-related tumor findings in males or females
  - 104-week diet studies in male and female Wistar rats: Hirose (1981)
    - No treatment-related tumor findings in males or females
  - 10-month diet studies in male and female C3H mice: Lindenschmidt (1986, p. 155)
    - Increase in liver tumors (by pairwise comparison) in males
    - No treatment-related tumor findings in females
- Two-generation diet studies in rats
  - Male and female Wistar rats dosed for entire lifespan: Olsen (1986, p 5)
    - Increase in hepatocellular adenoma, carcinoma, or adenoma and carcinoma combined (by pairwise comparison and trend) in males
    - Increase in hepatocellular adenomas (by pairwise comparison) in females
Other relevant data

- Genotoxicity: as reviewed in Bombard et al. (2002)
  - Mutagenicity tests with tester strains Salmonella typhimurium TA92, TA94, TA97, TA98, TA102, TA104, TA100, TA1530, TA1535, TA1537, TA1538, G46, E. coli (negative)
  - Sex-linked recessive lethal mutations in Drosophila melanogaster (negative)
  - Silk worm specific locus mutagenicity test (negative)
  - Mammalian point mutations HGPRT locus (negative)
  - Mouse lymphoma assay (positive)
  - In vivo specific locus test in mice (negative)
  - Chromosome abnormalities in onion (positive and negative), and barley and crepis (negative)
  - In Drosophila melanogaster, chromosome loss (positive), dominant lethal (negative), and reciprocal translocation (negative)
  - In vitro clastogenic and chromosomal aberrations in mammalian cells – human embryonic lung cells (positive for anaphase chromosomes), CHO (positive), Chinese hamster lung (negative)
  - In vivo clastogenic effects and chromosome aberrations, in rat bone marrow (negative), mouse micronuclei (negative), mouse germ cell (positive and negative), rat germ cell (negative)
  - DNA interactions, rec-assay (positive and negative), SOS-chromotest (negative), in vitro sister chromatid exchange in hamster lung, ovarian and DON cells (negative)

- Structure activity considerations
  - Structurally similar to butylated hydroxyanisole, a listed Proposition 65 carcinogen and IARC Group 2B carcinogen

- Modifies carcinogenicity
  - Tumor promoting activities in mouse lung: Thompson et al. (1989)
  - Tumor promoting activities in DBN, BBN, MNU-initiated urinary bladder carcinogenesis: Imaida (1983) as reviewed in Hirose et al. (1993)
  - Tumor promoting activities in DMH-initiated colon tumors in BALB/c mice (Lindenschmidt et al., 1986)

Reviews

- IARC (1986)
- IARC (1987)
References


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1 Excerpts or the complete publication have been provided to members of the Carcinogen Identification Committee, in the order in which they are discussed in this document.