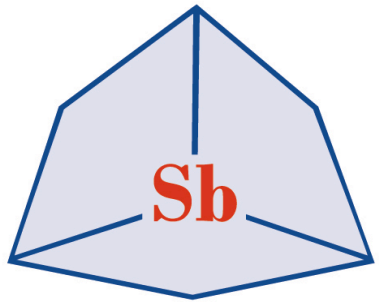

International
ANTIMONY
OXIDE
Industry Association

Antimony Trioxide (ATO) Comments on NTP Proposal to Assess Chronic Toxicity

James A. Deyo, D.V.M., Ph.D., D.A.B.T.
Eastman Chemical Company
June 13, 2006

Basis for Nomination by the NIEHS

- Substantial human exposure in occupational settings
  - Flame retardants
  - Transportation (brakes, batteries)
  - Paints/Ceramics
  - Plastics
- Non-occupational exposures
  - Food and drinking water (MCL = 6 ppb, WHO =20 ppb)
- Lack of adequate 2-year exposure studies by any route of exposure

ATO - Toxicological Database

- 90-Day oral toxicity: NOEL 5000 ppm (approx 450 mg/kg) with minimal toxicity at 20,000 ppm (NOAEL)
- In vitro genotoxicity data : Positive (clastogenicity); Negative (mutagenicity)
- In vivo genotoxicity data : Negative
- 3 Long term inhalation studies (1 year exposure with approx 1 year recovery before termination)
  - Newton et al. 1994 : No evidence of carcinogenicity in either sex at 5 mg/m3
  - Groth et al 1986 : Tumors seen in females only at 50 mg/m3.
  - Watt 1983 (Ph.D) thesis: Tumors seen in females (only sex tested) at 5 mg/m3, no tumors seen in swine

Comments

- Despite widespread consumer and workplace exposures by both inhalation and oral exposure routes, the current dataset lacks a well-conducted assessment of its carcinogenicity potential.
- The IAOIA would like to stress that chronic inhalation studies are needed to help clarify the contradictions in the current inhalation dataset with respect to the development of tumors in female rats only.

New Studies

- IAOIA supports the NTP's selection of ATO and believes there is a need for both chronic inhalation and oral studies.
- Inhalation studies need to be carefully conducted with respect to dose setting so as not to exceed the MTD for dust overload (Groth et al., 1986 and possibly Watt 1983 studies did exceed threshold for clearance impairment).
- New inhalation studies should include retention kinetics, and an evaluation of cellular genotoxic, inflammatory, and proliferative responses to help understand its potential MOA.