Overall Cancer Evaluation

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Summary of NTP’s preliminary conclusions

• A significant number of people living in the United States are or were exposed to antimony trioxide

• Studies in humans are inadequate for evaluating the relationship between human cancer and exposure to antimony trioxide and other antimony compounds

• Sufficient evidence of carcinogenicity for antimony trioxide from cancer studies in experimental animals
  – Multiple tissue sites in multiple species

• Supporting mechanistic information

• Biologically plausible in humans
Human exposure

• A significant number of people in the United States are exposed to antimony(III) trioxide

• Highest levels of exposure to antimony(III) trioxide occur in the workplace

• The general population is exposed to antimony
  – From some consumer products
  – From primary (i.e., pollutant is antimony(III) trioxide) and secondary (i.e., pollutant is transformed from other antimony species into antimony(III) trioxide) environmental releases
Inadequate human evidence for determining carcinogenicity

Limited by:

– Number of studies with small sample sizes for stomach and lung cancers.

– Potential confounding due to smoking and occupational co-exposures.
Sufficient animal evidence for antimony trioxide carcinogenicity

Increased incidences of malignant tumors and combined incidences of malignant and benign tumors at multiple tissue sites in multiple species.
Supporting mechanistic information

- Electrophilicity
- Affinity to vicinal thiol groups

Interact with
- Peptides (e.g., GSH)
- Proteins/ enzymes (including zinc finger)

Increase oxidative stress • $O_2^-$

Decrease DNA damage repair capacity

Cause receptor-mediated effects
e.g., Prevent cell differentiation → Preserve proliferation potential

Genotoxicity
- DNA damage
- Chromosomal aberrations
- Sister chromatid exchange
Cancer Evaluation: Integration of Animal, Human, and Mechanistic Data

- Comment on the overall cancer evaluation (Section 7: Overall Cancer Evaluation and Preliminary Listing Recommendation) and whether the available mechanistic data provide support for the relevance of the cancer studies in experimental animals to human carcinogenicity.
  - Provide any scientific criticism of the NTP’s overall assessment and integration of the human cancer, experimental animal, and mechanistic data.