Oral toxicity data for antimony - Annex 1 to TOX/2025/23

In this guide

In this guide

This is a draft position statement for discussion. This does not represent the views of the Committee and should not be cited.

Poon et al. 1998 study and interpretation

9. In the study by Poon et al. (1998), groups of 15 male and 15 female Sprague-Dawley rats were exposed to 0, 0.5, 5, 50, or 500 parts per million (ppm) antimony as antimony potassium tartrate (APT, 99.95% pure) in drinking water for 13 weeks. Based on average water consumption and body weight data, the investigators calculated antimony doses of 0, 60, 560, 5,580 and 42,170 µg/kg bw/day in males and 0, 60, 640, 6,130 and 45,690 µg/kg bw/day in females. An additional group of 10 male and 10 female rats was exposed to 0 or 500 ppm (0 and 42,170 µg/kg bw/day for males and 45,690 µg/kg bw/day for females) for 13

weeks followed by a 4-week recovery period.

10. A dose-dependent reduction (15–17%) in serum glucose levels in females exposed to doses greater than or equal to 640 µg Sb/kg bw/day was observed. Lower glucose values were also observed in the males; however, these were not statistically different from controls.

11. Other toxicological endpoints were identified by the study at the highest antimony doses in males and females (42,170 or 45,690 µg Sb/kg bw/day). These included a decrease in water and food consumption, a decrease in body weight gain (significant in males starting at week 6 and females at week 12), haematological changes which differed between males and females, decreases in serum creatinine levels and alkaline phosphatase levels, and liver effects including changes in activity of some liver enzymes such as ethoxyresorufin-O-deethylase (EROD) and glutathione-S-transferase (GST).

12. Anisokaryosis in the liver was observed in all antimony-exposed groups, with a dose-related increase in the severity observed.

13. Other hepatic effects included an increase in hepatocellular portal density in all antimony-exposed groups, but this was considered mild in males and females at greater than or equal to 560 and 640 µg Sb/kg bw/day respectively. Minimal nuclear hyperchromicity was also observed at these levels but with no consistent dose-response relationship.

14. In terms of skeletal effects, an increase in myeloid hyperplasia in the bone marrow was observed at ≥5,580 µg Sb/kg bw/day in males and ≥640 µg Sb/kg bw/day in females.

15. Spleen effects included sinus congestion at ≥560 µg Sb/kg bw/day in males, sinus hyperplasia at 42,170 µg Sb/kg bw/day in males and ≥640 µg Sb/kg bw/day in females and arterial cuff atrophy at 42,170 µg Sb/kg bw/day in males. In the recovery period, increases in incidence of sinus congestion (males only), arterial cuff atrophy, periarteriolar lymphocyte sheath cell density and sinus haematopoiesis were observed.

16. The study authors concluded 0.5 ppm antimony in drinking water, equivalent to an average intake of 60 µg Sb/kg bw/day, as the NOAEL for this study, primarily based on the statistically significant dose-dependent decrease in serum glucose levels in females at ≥640 µg Sb/kg bw/day.

17. Lynch et al. (1999) reviewed the Poon et al. (1998) study and provided an alternative interpretation of the observed toxicological effects. The authors stated that the observed effects at lower doses were either adaptive or non-toxicological in nature. They considered that some of the histological findings, particularly in the liver, spleen and thyroid, should not be considered toxicologically relevant and proposed a higher NOAEL. Lynch et al. (1999) proposed that the NOAEL for the study should be set at 50 ppm, equivalent to an average intake of 6,000 Sb µg/kg bw/day, based on the finding of decreased body weight gain and decreased food and water consumption at the 500 ppm dose level (though they stated that these effects may be due to the nonpalatability of the drinking water).

18. Valli et al. (2000), from the same group as Poon et al. (1998), maintained that the NOAEL of 60 µg/kg bw/day, as identified by Poon et al. (1998), was appropriate given the observed liver and spleen histology and serum biochemistry alterations. Valli et al. (2000) stated that the higher NOAEL of 6,000 µg/kg bw/day proposed by Lynch et al. (1999) underestimated the potential for early signs of toxicity and was not sufficiently protective.

Further oral antimony studies with NOAELs less than 6000 µg/kg bw/day

19. Marmo et al. (1987), Rossi et al. (1987) and Angrisani et al. (1988) reported findings from an antimony exposure study in NOS Albino normotensive rats.

20. Rossi et al. (1987) reported a NOAEL in maternal rats of 70 µg Sb/kg bw/day. This was due to a significant dose-dependent decrease in maternal body weight by gestation day 20 following prenatal oral exposure to antimony trichloride. It should be noted, however, that basal maternal body weights for each treatment group on day 0 of gestation prior to exposure were approximately 7% lower than the control group. Thus, the reported 8 to 10% deficit (in the low- and high- dose groups respectively) from controls seen on gestation day 20 represents a relatively small change from the 7% deficit at the start of gestation. The pup lowest observed adverse effect level (LOAEL) was reported as 700 µg Sb/kg bw/day due to decreases in body weight (Rossi et al., 1987).

21. Additional findings reported by Marmo et al. (1987) noted decreased vasomotor reactivity due to both prenatal and postnatal oral exposure to antimony trichloride. Additional findings reported by Angrisani et al. (1988)

showed postnatal exposure to antimony trichloride did not affect maternal or pup body weights or systolic arterial blood pressure.

22. In a study conducted by Kanisawa and Schroeder (1969), life term oral exposure to 5 ppm antimony as potassium tartrate (equivalent to 350 µg Sb/kg bw/day) in mice did not result in a significant difference in the incidences of spontaneous tumours or malignant tumours compared to controls. The authors identified 350 µg Sb/kg bw/day as the NOAEL for this study.

23. In a lifetime exposure study conducted by Schroeder et al. (1970), a significant reduction in survival rates and reduced non-fasting glucose levels were identified when rats were exposed to 430 µg Sb/kg bw/day potassium tartrate in their drinking water. The authors reported a LOAEL of 430 µg Sb/kg bw/day based on these effects.

24. Annex A provides further detail on the available antimony toxicity studies with comments on the Committees consideration of the reported NOAELs.