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In this guide

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16. 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 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 for 13 weeks followed by a 4-

week recovery period. The following parameters were used to assess toxicity: weekly body weight, food consumption and water intake measurements; haematological and clinical chemistry indices, serum thyroxin and thyroid hormone binding ratio; organ weights (brain, thymus, heart, kidney, spleen, liver); and histopathological examination (brain, pituitary, thyroid and trachea, salivary glands, thymus, lung, heart, liver, kidneys, adrenals, spleen, pancreas, oesophagus, stomach, small and large intestine, urinary bladder, skin, bone marrow and gonadal tissues).

17. No alterations in survival or overt signs of toxicity were observed. Decreases in water consumption (35% lower than controls) and food consumption (12%) were observed in the high dose (42,170/45,690 µg Sb/kg bw/day) group during the exposure period but not during the recovery period. A decrease in body weight gain, significant in males starting at week 6 and females at week 12, was observed at 42,170/45,690 µg Sb/kg bw/day; the body weights appeared to be within 10% of the controls. A significant increase in relative kidney weights was observed in the 42,170/45,690 µg Sb/kg bw/day group.

18. Haematological changes observed included a decrease in red blood cells and platelet counts, along with increase in mean corpuscular volume in males exposed to 42,170 µg Sb/kg bw/day. In females, the only haematological alteration was an increase in monocytes at 45,690 µg Sb/kg bw/day.

19. The serum chemistry changes included a dose-dependent reduction (15–17%) in serum glucose levels in females exposed to doses ≥640 µg Sb/kg bw/day; lower glucose values were also observed in the males, but were not statistically different from controls. No differences in serum glucose levels were observed at the end of the recovery period. Decreases in serum creatinine levels and alkaline phosphatase levels were noted in both males and females exposed to 42,170/45,690 µg Sb/kg bw/day at the end of the exposure period, but not at the end of the observation period. A decrease (24%) in serum cholesterol level and total protein were observed in females exposed to 45,690 µg Sb/kg bw/day; the toxicological significance of this alteration is not known.

20. In terms of liver effects, significant increases in hepatic ethoxyresorufin-O-deethylase (EROD) and glutathione-S-transferase (GST) activities were observed in males at 42,170 µg Sb/kg bw/day; glutathione-S-transferase activity was also increased in females at 45,690 µg Sb/kg bw/day. Histological alterations included anisokaryosis in the liver in all antimony-exposed groups, with dose-related increases in the severity observed. Anisokaryosis was also observed at the end of the recovery period. The severity scores for the anisokaryosis were 0.1, 0.6, 1.0,

1.9 and 2.8 in the 0, 60, 560, 5,580 and 42,170 µg Sb/kg bw/day males; a severity score of 1 is considered minimal, 2 is mild and 3 is moderate. In the females, the respective severity scores were 0.9, 1.5, 2.3, 2.3 and 2.6. Bridging fibrosis was observed in one animal of each sex in the highest dose group (42,170/45,690 µg Sb/kg bw/day in males/females).

21. Other hepatic effects included an increase in hepatocellular portal density in all antimony-exposed groups and minimal nuclear hyperchromicity at ≥560/640 µg Sb/kg bw/day, but there was not a consistent dose-response relationship for this endpoint. Similarly, the increase in portal density in the hepatocellular cytoplasm was graded as minimal at the two lowest doses in the males and females and mild at the two highest doses.

22. 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.

23. Spleen effects include 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.

24. Statistically significant increases in thyroid hormone binding ratio were observed in females at 6,130 and 45,690 µg Sb/kg bw/day. Thyroid histological alterations included an increase in epithelial height, reduced follicle size and nuclear vesiculation in antimony rats; an increased occurrence of collapsed follicles was observed in the antimony recovery group. These thyroid effects did not show a strong dose-response relationship and did not appear to affect thyroid function; the study authors did not consider these effects to be adverse.

25. The study authors concluded that 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.