

## Response from Valli et al. (2000)

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### Response from Valli et al. (2000)

29. In response to Lynch et al. (1999), Valli et al. (2000), which is the same group as Poon et al. (1998), re-affirmed the NOAEL of 60 µg/kg bw/day and emphasized the need to consider the full range of toxicological findings in the Poon et al. (1998) study. They responded that the histological changes have been observed, analysed and interpreted in conjunction with the serum biochemistry, haematology, tissue residue data and other changes in a fully appropriate manner.

- i. **Changes in the serum biochemical parameters:** Lynch et al. (1999) interpreted that lowering of serum glucose, cholesterol and alkaline

phosphatase were likely secondary to reduced caloric and water intake. Valli et al. (2000) responded that no clinical dehydration was observed in the antimony treated animals and no increase in serum albumin and haematocrit were observed in treated animals which might have been expected in clinical dehydration. Valli et al. (2000) did not respond to the comments by Lynch et al. (1999) that serum glucose estimation was conducted in non-fasted rats and potential confounding effect of reduced food intake on some of the observed serum biochemical changes.

ii. **Liver Findings:** Valli et al. (2000) acknowledged that anisokaryosis and hyperchromicity are commonly seen in young adult rats. However, they emphasized that these findings should not be dismissed, particularly given the concurrent significant decreases in alkaline phosphatase, serum creatinine and glucose as well as decreased serum cholesterol and total protein in high-dose females. They argued that the combination of histological changes and biochemical alterations suggested a functional impairment in the liver, warranting a more conservative NOAEL.

iii. **Spleen Findings:** Valli et al. (2000) acknowledged that spleen variations can occur under different circumstances, but they stressed that the changes noted were evaluated against spleens of concurrent vehicle controls and handled in exactly the same manner as far as anaesthesia and collection methods were concerned. They further emphasized that the interpretation of changes in the spleen is crucial, that antimony accumulates in red blood cells and because of the normal function of the spleen in removing senescent and injured blood cells, their accumulation might well be the basis for alterations in splenic histology as a result of exposure to APT.

iv. **Thyroid Findings:** Valli et al. (2000) agreed that there is normally much more variation in thyroid morphology in male rats as compared to females and as a result, females tend to be more reliable indicators of thyroid toxic effects at low levels of exposure. Further, since the thyroid gland is both a storage and an endocrine organ, it was not surprising that there was a considerable level of reserve thyroid globulin which is the reason that thyroxine levels may not change in the face of mild injury to the thyroid gland.

30. Valli et al. (2000) 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. They argued 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.