Discussion

In this guide

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29. The COT determined that the effects on serum glucose levels in female rats observed in Poon et al. (1998), which informed the NOAELs selected by ATSDR and Health Canada, showed limited dose-response. The Committee also noted that an intraperitoneal study by the National Toxicology Program (NTP) which examined antimony at higher doses and with greater bioavailability did not observe these effects (NTP 1992).

30. The Committee further agreed that the liver changes observed in Poon et al. (1998), which also informed the NOAEL selected by Health Canada, were minor and not indicative of adverse effects as there was no evidence of increase in liver weight across a large range of doses. The changes in the levels of liver enzymes were deemed to be minor and inconsistent with a hepatotoxic

effect. The Poon et al. (1998) study showed no clear evidence of changes in thyroid hormone effects and there was also difficulty in interpreting spleen findings due to high background variation and the findings were not considered to be of toxicological significance.

31. The Committee agreed with the Lynch et al. (1999) interpretation that the significant body weight changes observed at the highest dose in Poon et al. (1998) was critical effect. Therefore, the COT determined a NOAEL of 6,000 µg/kg bw/day for this study.

32. With respect to other oral studies with doses less than the NOAEL determined by COT for the Poon et al. (1998) study, the COT noted that the baseline maternal body weight in the study by Rossi et al. (1987) at gestation day 0 was approximately 7% lower in treated groups compared to controls. Consequently, the observed 8–10% reduction in maternal body weight at gestation day 20 used as the basis for the maternal NOAEL was considered a relatively small change, given the pre-existing baseline differences. The Committee noted that the NTP intraperitoneal study observed body weight effects only at the highest dose (9,600 µg Sb/kg bw/day).

33. The COT further observed that while decreased pup body weight was reported in the Rossi et al. (1987) study in the high dose group, the investigation by Angrisani et al. (1998) antimony exposure found no significant changes in pup body weight. With the lower initial maternal body weights in the treated groups reported in the Rossi et al. (1987) study, it was suggested that the observed lower body weight in prenatally exposed pups could be secondary to the lower maternal body weights of this group rather than a direct effect of antimony on pups. For these reasons, the lower NOAEL and LOAEL (when compared to the 6,000 µg Sb/kg bw/day NOAEL from the Poon et al. (1998) study) relating to maternal and pup body weight reported in the Rossi et al. (1987) study were discounted.

34. There were concerns regarding the reliability of the studies by Kanisawa and Schroeder (1969) and Schroeder (1970) and challenges interpreting their data. Furthermore, the nature of these studies does not allow for the demonstration of a dose-response, therefore the NOAELs and LOAELs reported in these studies were also discounted.