Discussion

In this guide

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74. The Committee noted that majority of laboratory animal oral toxicity data studies were undertaken between the 1960’s and the 1990’s, and there was limited human epidemiological evidence at levels of boron exposure expected from drinking water.

75. The Committee considered that the developmental toxicity study in rats by Price et al. (1996) was a good and well conducted multi-generational study, which identified a NOAEL of 9.6 mg/kg bw/day for reduced fetal body weight and skeletal malformations. The available oral toxicity data across the available studies were generally consistent and similar across species in identifying reduced fetal body weight, adverse effects in the testes and developmental malformations (e.g., skeletal malformations). The COT also considered that the NOAELs reported in the later oral toxicity studies were broadly consistent at approximately 10.0 mg B/kg bw/day, as far as could be

determined.

76. Several concerns were raised with respect to the Weir and Fisher, 1972 dog studies, and associated data undertaken in the 1960's by the Borax Research Corporation, which Health Canada had considered, but the COT had not further evaluated as they are not publicly available. The dog studies used a small sample size (approximately 4 per group) and provided no information on the age of the dogs. The Committee considered that this impaired the interpretation of the reported atrophy of the testes because the testicular epithelium could be incompletely developed in sexually immature dogs making it difficult to distinguish from testicular atrophy. Overall, the COT concluded that the dog oral toxicity studies were inadequate and not suitable for identifying a POD.

77. The Committee agreed with the broad consensus among authoritative bodies on using Price et al study as the basis for the POD (ECETOC, 1995; EFSA, 2013; EVM, 2003; WHO, 2009). Some authoritative organizations had used benchmark dose (BMD) modelling of the Price at al., (1996) study data, while others had used the NOAEL as a basis for their HBGV's. The COT noted that despite developments in BMD modelling, this made little difference to the resultant BMDL, and the BMDL and the study NOAEL were broadly similar. The Committee concluded that 10.0 mg B/kg bw/day was an appropriate POD, as had been concluded in the earlier COT assessment conducted in 1995.

78. In considering the uncertainty factor to use to derive a HBGV, the COT recognized that there had been consensus across several authoritative organizations in selecting a total uncertainty factor of approximately 60. However, the COT concluded that a total uncertainty factor of 100 was appropriate as this would account for the severity of the toxicity endpoints (reduced fetal weight and skeletal malformations), the extrapolation from animal to humans, and differences in toxicokinetics for different boron compounds. Applying a total uncertainty factor of 100, to the selected POD of 10.0 mg/kg bw/day would result in a TDI of 0.1 mg/kg bw/day.