European Borates Association A.I.S.B.L.
Member of IMA-Europe

EBA supplementary comments on CLH Report of 2 November 2018

Proposal for Harmonised Classification and Labelling of Boric acid; Diboron trioxide; Tetraboron disodium heptaoxide, hydrate; Disodium tetraborate, anhydrous; Orthoboric acid sodium salt; Disodium tetraborate decahydrate; Disodium tetraborate pentahydrate (hereafter refer to 'boron substances').

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The European Borates Association (EBA), on behalf of its members and on behalf of the REACH Borates Consortium, welcomes the opportunity to submit comments on the Swedish Chemicals Agency's CLH report.

SUPPLEMENTARY COMMENTS RELATED TO THE POTENCY MODIFYJNG FACTORS

Modifying factors are a means to account for case-specific data situations which indicate that the potency group for a substance, as obtained by the preliminary assessment, should be changed. The following modifying factors provide justification for placement of borates in the low potency group.

Epidemiological Data

Extensive toxicology testing in laboratory animals and high-quality studies of boron industry workers with chronic exposures to high levels of borates has been conducted. Although the toxicology studies show clear effects in laboratory animals, studies in boron industry workers show no effects when exposed to levels close to the NOAEL in rats. This shows that humans are not significantly more sensitive than rodents to the toxic effects of boric acid and may well be less sensitive.

Type of effect/Severity

Some effects are considered more severe than others. The effects of a developmental toxicant can differ between dose levels from variations via malformations to death of the fetuses. As noted in the guidance on the application of the CLP criteria, classification is in most cases based on severe effects like malformations or death of the fetuses for developmental toxicants and effects on fertility or histopathological changes of the reproductive organs for fertility toxicants.

The most sensitive developmental toxicity endpoints in Price et al (1996) were reduced fetal body weight, increased incidences of short rib XIII and wavy rib, and marginally decreased incidence of extra rib on lumbar I, all considered variations not malformations (Tyl et al 2004, 2007). Reductions in fetal body weight were dose-related and highly consistent across studies. The Price et al. (1996) study confirmed an earlier study (Heindel et al 1992) that 0.1% BA in feed as the LOAEL (76 mg/kg/day) and establishes 0.075% BA in feed (55 mg/kg/day, gd 0-20) as the NOAEL for reduction in live fetal body weight in the rat. However, during lactation, the offspring of BA-treated dams showed no growth retardation, indicating full recovery from a 12% prenatal weight deficit at the high dose (330 mg/kg). Postnatal recovery from reduced birth weight (94-76% of control weight on pnd 0) in rats exposed to 0.4-0.6% BA in the diet from gd 6-15 (NTP 1994, Price et al. 1996) supports

the conclusion that offspring can readily recover from the level of body weight reduction encountered in this study.

The CLH proposal identified the most sensitive effect on development by boric acid is the increased incidence of short rib XIII. Short rib XIII (< 0.5 the length of rib XII) was classified as a malformation in the earlier studies (Heindel et al. 1992) and considered a malformation by Sweden in the CLH proposal. However, elsewhere this finding is classified as a variation since short rib XIII occurs spontaneously in some control fetuses and has no effect per se upon viability or function. Short Rib XIII has been shown to be reversible after 21 days (Marr et al. 1992 in Price et al. 1996). The incidence of short rib XIII, which was elevated significantly by 0.1% boric acid in fetuses examined at GD20, was elevated only at the highest dose 0.2% when offspring were examined at PND 21, suggesting some degree of recovery or repair. Likewise, wavy ribs observed in fetuses of dams fed boric acid were not observed in the postnatal cohort. Further, no extra lumbar ribs were observed in pups at PND 21 (Tyl et al. 2007; Tyl et al. 2004).

Since the effects that the ED10/LOAEL was based on to place boric acid in the medium potency group are considered variations that have no effect upon viability or function that are largely reversible. The effects are not considered severe and should not be used as criteria for potency class.

Male Fertility Effects

The LOAEL for fertility effects in rats is 334 mg BA/kg bw/day based on data from the lifetime 2-year feeding study with boric acid in rats, near the upper end of the medium potency group (Weir & Fisher 1972). The LOAEL of a 90-day feeding study of boric acid based on effects in the testes was 502 mg BA/kg/bw/day, in the low potency group (Paynter 1962). The LOAEL in a 2-year feeding study in rats for disodium tetraborate decahydrate is 516 mg /kg bw/day, within the low potency group (Weir & Fisher 1972). As noted previously, although below the NOAELs in studies of laboratory animals, no adverse effects were observed in epidemiological studies in highly exposed workers and populations exposed to high levels for many years. This provides supporting data for low potency of boric acid and other borates.

CONCLUSION

Based on modifying factors, there is adequate and reliable scientific information that a hazard of boric acid and other borates is more aligned with the low potency group.

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