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Butyl Benzyl Phthalate (BBP)

Summary

Food Safety Commission of Japan

The Food Safety Commission of Japan (FSCJ) conducted a risk assessment of butyl benzyl phthalate (BBP) (CAS No.85-68-7) for the revision of the standards and criteria for apparatuses, containers and packages. Major adverse effects of BBP observed are those on body weight, pancreas, liver, kidney, and also on reproduction and development of offspring. FSCJ judged that BBP has no genotoxicity relevant to human health based on the results of genotoxicity studies, and thus judged it to be able to set tolerable daily intake (TDI) on this chemical. Dose-response relationship for human exposure to BBP was unable to obtain from the epidemiological studies, due to the lack of consistency among the results. FSCJ thus concluded it appropriate to specify TDI based on the results of studies in experimental animals rather than the epidemiological data. Similar to the case of bis (2-ethylhexyl) phthalate (DEHP) and dibutyl phthalate (DBP), toxicities toward the offsprings are the most sensitive and critical endpoints for TDI specification. FSCJ concluded it appropriate to establish an overall no-observed-adverse-effect level (NOAEL) of 20 mg/kg bw/day from three available studies on two-generation reproductive toxicity, which were adequately designed. In conclusion, FSCJ specified the TDI of 0.2 mg/kg bw, applying an uncertainty factor of 100 (10 for species difference, 10 for individual difference) to the NOAEL of 20 mg/kg bw/day.

Conclusion in Brief

The Food Safety Commission of Japan (FSCJ) conducted a risk assessment of butyl benzyl phthalate (BBP) (CAS No.85-68-7) for the revision of the standards and criteria for apparatuses, containers and packages.

The data used in the assessment include toxicokinetics (rats, dogs and humans), acute toxicity (rats), subacute toxicity (rats and dogs), chronic toxicity and carcinogenicity (mice and rats), reproductive and developmental toxicity (mice, rats and rabbits), and genotoxicity.

Major adverse effects of BBP observed are those on body weight, pancreas, liver, kidney, and also on reproduction and development of offspring. Reduced weights of testes and epididymides, seminiferous tubular atrophy, reduced testicular sperm counts and disrupted blood hormone levels such as decreased serum concentration of testosterone were observed as BBP influences in the reproductive organs of male animals. Reduced ovarian weight was observed as a BBP effect on female parental animals. Decreased fertility rates and increased postimplantation loss rates were also observed. Clear adverse effects of *in utero* exposure to BBP observed were decreased survival rate, lowered body weights, decreased anogenital distance (AGD) of male offsprings and reduced weights of the testes and epididymides, as well as increased AGD in female offsprings.

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Neoplastic lesions were not observed in mice. An increased incidence of mononuclear cell leukemia was, however, observed in female rats in carcinogenicity studies. Incidence of pancreatic acinar-cell adenomas was increased in male rats in chronic toxicity and carcinogenicity studies.

FSCJ judged that BBP has no genotoxicity relevant to human health based on the results of genotoxicity studies, and thus judged it to be able to set tolerable daily intake (TDI) on this chemical.

Dose-response relationship for human exposure to BBP was unable to obtain from the epidemiological studies, due to the lack of consistency among the results. FSCJ thus concluded it appropriate to specify TDI based on the results of studies in experimental animals rather than the epidemiological data.

Similar to the case of bis (2-ethylhexyl) phthalate (DEHP) and dibutyl phthalate (DBP), toxicities toward the offsprings are the most sensitive and critical endpoints for TDI specification. Consequently, TDI of BBP was specified based on the data from three available studies on two-generation reproductive toxicity, which were adequately designed. In the reviewing processes of the three studies, FSCJ specifically focused on the mutual effects such as decreased AGD and lowered body weights seen in offspring: decreased AGD was observed at 250 mg/kg bw/day (no-observed-adverse-effect level (NOAEL) 50 mg/kg bw/day) with Tyl et al[1)], decreased AGD and lowered body weights were at 500 mg/kg bw/day and 100 mg/kg bw/day, respectively, (NOAEL 20 mg/kg bw/day) with Nagao et al[2)], and decreased AGD and lowered body weights were at 100 mg/kg bw/day (lowest-observed-adverse-effect level (LOAEL)) with Aso et al[3)]. From these data, the observed effect at the LOAEL dose of 100 mg/kg bw/day of Aso et al[3)] suggests the necessity of careful consideration for NOAEL determination. FSCJ, therefore, concluded it appropriate to establish an overall NOAEL of 20 mg/kg bw/day.

In conclusion, FSCJ specified the TDI of 0.2 mg/kg bw, applying an uncertainty factor of 100 (10 for species difference, 10 for individual difference) to the NOAEL of 20 mg/kg bw/day obtained in the two-generation reproductive toxicity studies in rats.

References

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