FOOD SAFETY

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Dibutyl Phthalate (DBP)

Summary

Food Safety Commission of Japan

The Food Safety Commission of Japan (FSCJ) conducted a risk assessment of dibutyl phthalate (DBP) (CAS No.84–74-2) for the revision of the standards and criteria for apparatuses, containers and packages. DBP showed major adverse effects on liver and kidney, and also showed the reproductive and developmental toxicities (mice, rats and rabbits). The reproductive toxicities were observed in both sexes of experimental animals (mice and rats). No consistent results were obtained on human epidemiological studies, although some data suggested the possible association of DBP exposures with toxicological parameters including reproductive/developmental systems No definitive studies on carcinogenicity and chronic toxicity were available with DBP in experimental animals. No clear information is thus available on the carcinogenic effects of DBP in humans to date. FSCJ judged that DBP has no genotoxicity relevant to human health. Therefore, it is appropriate to specify a tolerable daily intake (TDI) based on the results of reproductive-developmental toxicity studies in experimental animals. Among the test values for the no-observed-adverse-effect level (NOAEL) or the lowest-observed-adverse-effect level (LOAEL), the lowest value was the LOAEL of 2.5 mg/kg bw/day in a dietary toxicity study in rats. FSCJ judged it appropriate to apply an uncertainty factor of 500 (10 for species difference, 10 for individual difference, and additional 5 for the use of the LOAEL) to the LOAEL (0.25 mg/kg bw/day) and specified the TDI of 0.005 mg/kg bw/day.

Conclusion in Brief

The Food Safety Commission of Japan (FSCJ) conducted a risk assessment of dibutyl phthalate (DBP) (CAS No.84–74-2) for the revision of the standards and criteria for apparatuses, containers and packages.

The data used in the assessment include acute toxicity (rats and mice), subacute toxicity (rats and mice), carcinogenicity (mice and rats), reproductive and developmental toxicity (rats, mice, and rabbits), genotoxicity and epidemiological studies.

DBP showed major adverse effects on liver and kidney, and also showed the reproductive and developmental toxicities (mice, rats and rabbits). The reproductive toxicities were observed in both sexes of experimental animals (mice and rats). Even in low doses, adverse effects on the reproductive organ appeared in male offsprings of rats after *in utero* and/or neonatal exposures to DBP. No consistent results were obtained on human epidemiological studies, although some data suggested the possible association of DBP exposures with toxicological parameters including reproductive/developmental systems.

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No definitive studies on carcinogenicity and chronic toxicity were available with DBP in experimental animals. International Agency for Research on Cancer (IARC) classifies DBP in the category of inadequate evidence in humans for carcinogenicity.

United States Environmental Protection Agency (USEPA) lists DBP as Group D, not classifiable as to human carcinogenicity.

No clear information is thus available on the carcinogenic effects of DBP in humans to date.

FSCJ judged that DBP has no genotoxicity relevant to human health. Therefore, it is appropriate to specify a tolerable daily intake (TDI) based on the results of reproductive-developmental toxicity studies in experimental animals.

Among the values for the no-observed-adverse-effect level (NOAEL) or the lowest-observed-adverse-effect level (LOAEL), the lowest value was the LOAEL of 2.5 mg/kg bw/day in a dietary toxicity study in rats. The vacuolar degeneration and atrophy of mammary gland alveoli in male rats were observed continually even at postnatal week (PNW) 20, while the retardation of development involving mammary alveolar buds in the females and loss of germ cell development (spermatogonia to spermatocyte) in the males were reversed to normal at PNW 11. Taking these findings into account, FSCJ judged it appropriate to apply an uncertainty factor of 500 (10 for species difference, 10 for individual difference, and additional 5 for the use of the LOAEL).

Consequently, FSCJ specified the TDI of 0.005 mg/kg bw/day.