This is a provisional English translation of an excerpt from the original full report.

# Risk Assessment Report

## Diisononyl Phthalate (DINP)

(Apparatuses, Containers and Packages)

Food Safety Commission of Japan (FSCJ)
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## ABSTRACT

FSCJ conducted a risk assessment of diisononyl phthalate (DINP) (CAS No. 68515-48-0 and 28553-12-0) for the revision of the standards and criteria for apparatuses, containers and packages.

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

On the basis of the data from comparable studies on DINP-1 (CAS68515-48-0), DINP-2 (CAS 28553-12-0) and DINP-3 (CAS 28553-12-0), FSCJ considered it appropriate to evaluate the safety risk of these three products in a combined assessment without distinguishing their products because of similarlity of their toxicological effects *in vivo*.

Results from various toxicity studies indicated the relatively week acut toxicity on DINP and that the target organs of its chronic/carcinogenic toxicity were the liver (gain of absolute and relative weights, spongiosis hepatis and localized necrosis) and kidney (gain of absolute and relative weights). Develomental toxicity of DINP on the second generation was mainly observed as low body weight, decreased birth rate and survival rate, skeletal and visceral variations such as Lumbar Rib, and also on tissues of genitalia such as seminiferous tubule.

In chronic toxicity- and carcinogenicity-combined studies in Fischer 344 rats, increased incidence of mononuclear cell leukemia (MNCL) in both the male and female and of kidney cancer in the male were observed. MNCL is, however, a strain specific effects on Fischer 344 rats, and the incidence rates of the kidney cancer was not significant. In addition, kidney cancer induced by an accumulation of α2u groblin has been known to be a male specific effect. FSCJ considered that these neoplastic lesions are not significant for assessment of risk to human health.
DINP has no genotoxicity relevant to human health based on the results of the genotoxicity study. FSCJ thus judged it possible to establishe the TDI.

Both positive and negative associations have been observed between epidemiological endpoints and levels of DINP and monoisononyl phtarate (MINP) or its oxide in urine, serum or breast milk. FSCJ considered that these epidemiological data are insufficient as the basis for estimating an association between the human exposure and the health effects because of the limited number of reported data on each endpoint.
FSCJ concluded that it is appropriate to establish the TDI of DINP based on the data from animal studies

as mentioned above.

Among the test values for the no-observed-adverse-effect-level (NOAEL), the lowest NOAEL of DINP was obtained in the chronic toxicity/carcinogenicity combined study in Fischer 344 rats (Lington et al., 1977). Main target olgans of the effect observed in the relevant study was the liver and kidney, giving NOAEL of 15 mg/kg bw/day in male and 18 mg/kg bw/day in female.

Consequently, FSCJ specified the TDI of 0.15 mg/kg bw/day by applying Uncertainty Factor of 100 to the NOAEL of 15 mg/kg bw/day.