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

Risk Assessment Report

Dichloroisocyanuric acid

(Veterinary Medicinal Products)

Food Safety Commission of Japan (FSCJ)
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ABSTRACT

FSCJ conducted a risk assessment of a disinfectant, dichloroisocyanuric acid (CAS No. 2782-57-2), based on toxicity test reports and documents of EPA, OECD, JECFA and EFSA.

Dichloroisocyanuric acid is one of chlorinated isocyanuric acids that are rapidly hydrolyzed to isocyanuric acid after contact with water or saliva. Therefore, FSCJ conducted assessment of dichloroisocyanuric acid using data on chlorinated isocyanuric acids including dichloroisocyanuric acid and trichloroisocyanuric acid, and its sodium salts, as well as isocyanuric acid and cyanuric acid and its sodium salts.

Data of all genotoxicity studies suggested that dichloroisocyanuric acid and isocyanuric acid have no genotoxicity relevant to human health. Consequently, FSCJ concluded that the acceptable daily intake (ADI) for dichloroisocyanuric acid and isocyanuric acid could be specified.

Among various toxicity studies, damage to renal or urinary tract including stone formation and urothelial hyperplasia of the bladder mucosa was observed in the subacute toxicity studies of isocyanuric acid and sodium cyanurate in rats and mice,
Carcinogenicity was not observed in mice and rats exposed to sodium cyanurate through drinking water in carcinogenicity studies.
Isocyanulic acid had no effects on reproduction of parental male and female in rats and on the development of newborns in reproductive and developmental toxicity studies by gavage.
In three-generation reproduction study, no effect on reproduction and on offspring were observed after exposure to sodium isocyanurate through drinking water. In addition, sodium cyanurate to rats and of sodium isocyanurate to rabbits in developmental toxicity studies showed no teratogenicity and fetotoxicity.
Since dichloroisocyanurate is rapidly hydrolyzed to isocyanuric acid after contact with water or saliva, FSCJ considered a residue substance to which human has a potential to be exposed through foods is isocyanuric acid as long as it is used appropriately to disinfect livestock and chicken. Accordingly, FSCJ judged it more reliable that the acceptable daily intake (ADI) for dichloroisocyanuric acid is

specified based on the results to toxicity studies of isocyanuric acid, cyanuric acid and their sodium salts.

Among all the studies, the adverse effect observed at the lowest dose was urothelial hyperplasia of the bladder mucosa in male rats in the 13-week subacute toxicity study of sodium cyanurate administered through drinking water. The NOAEL was 101 mg/kg body weight/day.
FSCJ concluded that this value was appropriate to the ADI of dichloroisocyanuric acid as 0.86 mg/kg bw/day (converted into isocyanuric acid) applying safety factor of 100 to the NOAEL.

Table 1. *Levels relevant to toxicological evaluation of dichloroisocyanuric acid*

Assessed item	Species	Study	Test substance	Dose (mg/kg bw/day)	NOAEL (mg/kg bw/day) and Critical endpoints[1]			
					OECD	JECFA	EFSA	FSCJ
Dichloroisocyanuric acid	Mouse	Reproductive developmental toxicity	Sodium dichloroisocyanurate	0, 25, 100, 400 (oral gavage)		Not judged		NOAEL Dams: 100 Increased mortality Fetuses: 400 No teratogenicity
	Rat	13-week subacute toxicity	Sodium dichloroisocyanurate	0, 3, 30, 300 (oral gavage)				NOAEL M/F: 30 Suppressed body weight, decreased feed intake
Isocyanuric acid	Mouse	13-week subacute toxicity	Sodium cyanurate monohydrate	0, 896, 1 792, 5 375 ppm (drinking water)	NOAEL (cyanuric acid) M: 1 994 (5 375 ppm) F: 2 200 (5 375 ppm)	NOEL (cyanuric acid) M: 522 (1 792 ppm) Bladder stones	NOEL (cyanuric acid) M: 522 (1 792 ppm) Bladder stones	NOAEL (cyanuric acid) M: 522 (1 792 ppm) Bladder stones (Urothelial hyperplasia , with congestion/ bleeding) F: 2 200 (5 375 ppm) No toxicity
		104-week Carcinogenicity	Sodium cyanurate	0, 100, 400, 1 200, 5 375 ppm (drinking water)	No carcinogenicity	No carcinogenicity	No carcinogenicity	NOAEL M: 1 523 (5 375 ppm) F: 1 582 (5 375 ppm) No carcinogenicity
	Rat	Combined repeated oral	Isocyanuric acid	0, 10, 40, 150, 600	NOAEL M/F: 150		Not judged	NOAEL M/F: 150

[1] Major adverse effect observed at LOAEL

		dose/reproductive developmental toxicity		(oral gavage)	Injury of the kidney, epithelial hyperplasia of the bladder mucosa Dams: 600 Newborn: 600			Injury of the kidney, Urothelial hyperplasia of the bladder mucosa Dams: 600 Newborn: 600 No effects on reproductive activity of parent animals and development of newborns
		13-week subacute toxicity	Sodium cyanurate monohydrate	0, 896, 1 792, 5 375 ppm (drinking water)		NOEL M: 72 (896 ppm) Epithelial hyperplasia of the bladder mucosa F: 496 (1 792 ppm)	Not judged	NOAEL M: 101 (896 ppm) Urothelial hyperplasia of the bladder mucosa F: 870 (5 375 ppm) No toxicity
		104-week carcinogenicity	Sodium cyanurate	0, 400, 1 200, 2 400, 5 375 ppm (drinking water)	No carcinogenicity	NOEL M: 154 (2 400 ppm) Urinary tract, heart lesion No carcinogenicity	NOEL M: 154 (2 400 ppm) Urinary tract, heart lesion	NOAEL M: 154 (2 400 ppm) Decreased survival rate, the kidney, urinary tract and heart lesion F: 266 (2 400 ppm) Urinary calculi No carcinogenicity
		Developmental toxicity	Sodium cyanurate	0, 200, 1 000, 5 000 (oral gavage)	NOAEL Developmental toxicity: 5 000	Not judged	Not judged	Dams: 5 000 Fetuses: 5 000 No teratogenicity
		Three-generation reproduction	Sodium isocyanurate	0, 400, 1 200, 5 375 ppm (drinking water)	NOAEL Reproductive toxicity: 5 375 ppm	NOEL Reproductive toxicity: 5 375 ppm		NOAEL Parent M: 109 (1 200 ppm) Bladder stones F: 450 (5 375 ppm) No toxicity Reproductive toxicity: PM: 612, F_1M: 666, F_2M:563, FP:769, FF_1: 450, FF_2: 971 (5 375 ppm)

								No effects on reproductive activity and on fetuses.
	Rabbit	Developmental toxicity	Sodium isocyanurate	0, 50, 200, 500 (oral gavage)	NOAEL Developmental toxicity: 200 Fetuses: Decreases in body weight and crown-rump length		Not judged	NOAEL Developmental toxicity: 500 No toxicity
		Developmental toxicity	Sodium isocyanurate	0, 50, 200, 500 (oral gavage)		Not judged		NOAEL Dams: 50 Suppressed body weight or decreased body weight (slightly)
Toxicological TDI/ADI (mg/kg bw/day)						TDI: 0~2.0	TDI: 1.5	ADI: 0.86 (as isocyanuric acid)
The critical study for setting Toxicological TDI/ADI						104 carcinogenicity study of sodium cyanurate in rats	104 carcinogenicity study of sodium cyanurate in rats.	13-week subacute toxicity study of sodium cyanurate in rats.
TDI/ADI (mg/kg bw/day)						TDI: 0~2.0	TDI: 1.5	ADI: 0.86 (as isocyanuric acid)