Table 3 Incidence of clinical signs of male rats treated orally with isocyanuric acid in the combined repeat dose and reproductive/developmental toxicity screening test

Clinical sign	Dose(mg/kg)	0		10			40			150		600	
	Fate	TK	(Total)	TK	FP	(Total)	TK	UC	(Total)	TK	(Total)	TK	(Total)
	No. of animals	10	(10)	8	2	(10)	9	1	(10)	10	(10)	10	(10)
Reddish urine		0	(0)	0	0	(0)	0	0	(0)	0	(0)	9	(9)**
Chromodacryorrhea		0	(0)	0	0	(0)	1	0	(1)	1	(1)	0	(0)
Ptosis		0	(0)	0	0	(0)	0	0	(0)	1	(1)	0	(0)
Alopecia		0	(0)	0	0	(0)	0	0	(0)	1	(1)	0	(0)
Loss of upper incisors		0	(0)	0	0	(0)	1	0	(1)	0	(0)	0	(0)

TK : Terminal kill

UC : Animal with unsuccessful copulation

FP : Failed to cause pregnancy, killed at the termination

** : Significantly different from control at 1 % level of probability

Table 4 Incidence of clinical signs of female rats treated orally with isocyanuric acid in the combined repeat dose and reproductive/developmental toxicity screening test

Clinical sign	Dose(mg/kg)	0		10			40				150			600	
	Fate	TK	(Total)	TK	NP	(Total)	TK	UC	KL	(Total)	TK	KL	(Total)	TK	(Total)
	No. of animals	10	(10)	8	2	(10)	8	1	1	(10)	9	1	(10)	10	(10)
Emaciation		0	(0)	0	0	(0)	0	0	0	(0)	0	0	(0)	4	(4)*
Reddish urine		0	(0)	0	0	(0)	0	0	0	(0)	0	0	(0)	3	(3)
Decrease in locomotor activity/ piloerection/hypothermia		0	(0)	0	0	(0)	0	0	0	(0)	0	0	(0)	1	(1)
Soiled fur		0	(0)	0	0	(0)	0	0	0	(0)	0	0	(0)	2	(2)
Alopecia/scabbing		0	(0)	0	0	(0)	0	0	0	(0)	1	0	(1)	1	(1)

TK : Terminal kill

NP : Non-pregnant, killed on 26 days after copulation

UC : Animal with unsuccessful copulation

KL : Killed because all pups died after delivery

* : Significantly different from control at 5 % level of probability

Table 5 Body weights of male rats treated orally with isocyanuric acid in the combined repeat dose and reproductive/developmental toxicity screening test

(g)

Dose (mg/kg)	Days of treatment								
	1	8	15	22	29	36	43	44	Gain 1~44
0	343 ± 13 (10)	376 ± 21 (10)	408 ± 28 (10)	435 ± 30 (10)	463 ± 35 (10)	490 ± 40 (10)	503 ± 45 (10)	505 ± 44 (10)	163 ± 33 (10)
10	343 ± 13 (10)	390 ± 15 (10)	431 ± 14 (10)	458 ± 15 (10)	490 ± 16 (10)	511 ± 15 (10)	525 ± 22 (10)	528 ± 22 (10)	185 ± 20 (10)
40	343 ± 12 (10)	383 ± 21 (10)	420 ± 26 (10)	449 ± 26 (10)	478 ± 27 (10)	502 ± 29 (10)	511 ± 36 (10)	514 ± 36 (10)	171 ± 27 (10)
150	343 ± 11 (10)	385 ± 11 (10)	422 ± 19 (10)	443 ± 26 (10)	475 ± 27 (10)	499 ± 36 (10)	514 ± 40 (10)	518 ± 42 (10)	174 ± 34 (10)
600	344 ± 12 (10)	358 ± 30 (10)	391 ± 25 (10)	402* ± 20 (10)	425** ± 18 (10)	453* ± 25 (10)	461* ± 30 (10)	464* ± 33 (10)	120** ± 27 (10)

Each value is expressed as mean±S.D. and (number of animals examined).
* : Significantly different from control at 5% level of probability
** : Significantly different from control at 1% level of probability

Table 6 Body weights of female rats treated orally with isocyanuric acid in the combined repeat dose and reproductive/developmental toxicity screening test

(g)

Dose (mg/kg)	Days of premating				Days of pregnancy					Days of lactation		
	1	8	15	Gain 1~15	0	7	14	20	Gain 0~20	0	4	Gain 0~4
0	223 ± 5 (10)	246 ± 10 (10)	265 ± 13 (10)	43 ± 11 (10)	271 ± 11 (10)	311 ± 11 (10)	353 ± 12 (10)	451 ± 16 (10)	180 ± 10 (10)	330 ± 22 (10)	345 ± 16 (10)	15 ± 16 (10)
10	223 ± 5 (10)	240 ± 10 (10)	258 ± 11 (10)	36 ± 10 (10)	265 ± 16 (8)	302 ± 13 (8)	344 ± 15 (8)	436 ± 18 (8)	171 ± 12 (8)	316 ± 24 (8)	336 ± 17 (8)	21 ± 17 (8)
40	222 ± 5 (10)	247 ± 9 (10)	263 ± 11 (10)	41 ± 9 (10)	273 ± 7 (9)	314 ± 6 (9)	359 ± 8 (9)	456 ± 13 (9)	182 ± 16 (9)	338 ± 28 (9)	359 ± 14 (8)	16 ± 20 (8)
150	223 ± 4 (10)	245 ± 7 (10)	262 ± 9 (10)	39 ± 6 (10)	274 ± 13 (10)	308 ± 10 (10)	346 ± 15 (10)	432 ± 34 (10)	157 ± 31 (10)	343 ± 18 (10)	350 ± 16 (9)	4 ± 10 (9)
600	222 ± 5 (10)	227 ± 28 (10)	252 ± 19 (10)	30 ± 17 (10)	261 ± 17 (10)	291 ± 23 (10)	337 ± 19 (10)	429 ± 26 (10)	168 ± 18 (10)	309 ± 27 (10)	307 ± 38 (10)	-2 ± 25 (10)

Each value is expressed as mean±S.D. and (number of animals available).

Table 7 Food consumption of male rats treated orally with isocyanuric acid in the combined repeat dose and reproductive/developmental toxicity screening test

(g/rat/day)

Dose (mg/kg)	Days of treatment					
	1	8	22	29	36	43
0	24 ± 2 (10)	27 ± 4 (10)	28 ± 3 (10)	28 ± 3 (10)	29 ± 3 (10)	27 ± 2 (10)
10	25 ± 2 (10)	30 ± 2 (10)	27 ± 1 (10)	28 ± 3 (10)	27 ± 3 (10)	26 ± 2 (10)
40	25 ± 3 (10)	28 ± 3 (10)	27 ± 2 (9)	27 ± 2 (10)	24 ± 8 (10)	26 ± 4 (10)
150	24 ± 2 (10)	28 ± 4 (10)	28 ± 2 (10)	28 ± 4 (10)	27 ± 3 (10)	28 ± 4 (10)
600	18 ±10 (10)	24 ± 6 (10)	24 ± 7 (10)	24 ± 5 (10)	28 ± 3 (10)	27 ± 5 (10)

Each value is expressed as mean±S.D. and (number of animals examined).

Table 8 Food consumption of female rats treated orally with isocyanuric acid in the combined repeat dose and reproductive/developmental toxicity screening test

(g/rat/day)

Dose (mg/kg)	Days of premating		Days of pregnancy				Days of lactation	
	1	8	0	7	14	20	0	3
0	19 ± 3 (10)	20 ± 3 (10)	20 ± 3 (10)	25 ± 3 (10)	28 ± 3 (10)	23 ± 3 (10)	14 ±10 (10)	52 ± 8 (10)
10	17 ± 3 (10)	20 ± 3 (10)	19 ± 2 (8)	25 ± 3 (8)	25 ± 3 (8)	23 ± 4 (8)	17 ±11 (8)	49 ± 3 (8)
40	17 ± 3 (10)	21 ± 3 (10)	20 ± 4 (9)	26 ± 3 (9)	27 ± 3 (9)	25 ± 4 (9)	15 ±10 (9)	49 ± 6 (8)
150	18 ± 3 (10)	20 ± 4 (10)	20 ± 2 (10)	24 ± 3 (10)	26 ± 2 (10)	25 ± 3 (10)	11 ± 7 (9)	42 ±12 (9)
600	16 ± 5 (10)	19 ± 6 (10)	15 ± 4 (10)	23 ± 7 (10)	27 ± 4 (10)	22 ± 7 (10)	12 ±11 (10)	37 ±22 (10)

Each value is expressed as mean±S.D. and (number of animals available).

Table 9 - 1 Urinary findings of male rats treated orally with isocyanuric acid in the combined repeat dose and reproductive/developmental toxicity screening test

Dose (mg/kg)	No. of animals	Color				Cloudy		Specific gravity	pH							Protein					
		C	PY	Y	PB	−	+		5.0	6.0	6.5	7.0	7.5	8.0	8.5	−	±	+	++	+++	++++
0	10		4	3	3	7	3	1.050 ± 0.021 a)			1	1	1	2	5		2	6	2		
10	10		3	5	2	5	5	1.068 ± 0.031			1		4	5				5	4	1	
40	10		4	5	1	3	7	1.051 ± 0.019			2	2		4	2			10			
150	10	1	5	2	2		10**	1.056 ± 0.018				2	3	2	3			5	5		
600	10		9		1	1	9*	1.033 ± 0.012		1	1	4	1	3			1	9			

Dose (mg/kg)	No. of animals	Glucose					Ketone body					Occult blood					Urobilinogen				Bilirubin			
		−	±	+	++	+++	−	±	+	++	+++	−	±	+	++	+++	0.1	1	2	4	−	+	++	+++
0	10	10					4	4	1	1		7	3				10				10			
10	10	10					1	6	3			9	1				10				10			
40	10	10					5	5				8	2				10				10			
150	10	10					2	7	1			9	1				10				10			
600	10	10					6	4				7		1	1	1	10				10			

a) : Mean±S.D.
Color : C(colorless), PY(pale yellow), Y(yellow), PB(pale brown)
Cloudy : −(negligible), +(cloudy)
Protein : −(negligible), ±(15～30mg/dl), +(30mg/dl), ++(100mg/dl), +++(300mg/dl), ++++(1000mg/dl)
Glucose : −(negligible), ±(0.1g/dl), +(0.25g/dl), ++(0.5g/dl), +++(1g/dl)
Ketone body : −(negligible), ±(5mg/dl), +(15mg/dl), ++(40mg/dl), +++(80mg/dl)
Occult blood : −(negligible), ±(trace), +(slight), ++(moderate), +++(marked)
Urobilinogen : Ehrlich unit/dl
Bilirubin : −(negligible), +(slight), ++(moderate), +++(marked)
* : Significantly different from control at 5% level of probability
** : Significantly different from control at 1% level of probability

Table 9 - 2 Urinary findings of male rats treated orally with isocyanuric acid in the combined repeat dose and reproductive/developmental toxicity screening test

Dose (mg/kg)	No. of animals	Erythrocytes				Leukocytes				Crystals: Mg				Ca		Ams		Others			
		−	+	++	+++	−	+	++	+++	−	+	++	+++	−	+	−	+	−	+	++	+++
0	10	10				10				1	4	4	1	10		10		10			
10	10	10				9	1			2	2	5	1	10		10		10			
40	10	10				10				4		4	2	10		10		6	3	1	
150	10	10				10				1	3	5	1	10		10			5	3	2**
600	10	7	1	1	1*	5	1	4**		4	3	3		10		10		2	5	2	1**

Dose (mg/kg)	No. of animals	Epithelial cells: Sq				R			S			Casts: G		H		W		Fat globules		
		−	+	++	+++	−	+	++	−	+	++	−	+	−	+	−	+	−	+	++
0	10	1	8	1		10			10			10		10		10		10		
10	10	1	4	5		10			10			10		10		10		10		
40	10	1	9			10			10			10		10		10		10		
150	10		9	1		10			10			10		10		10		10		
600	10		10			10			10			10		10		10		10		

− : Not observed; + : A few in some fields; ++ : A few in all fields; +++ : Many in all fields

Crystals
- Mg(ammonium magnesium phosphate)
- Ca(calcium phosphate)
- Ams(amorphous)
- Others(crystals considered to be the test substance precipitated from urine)

Epithelial cells
- Sq(squamous)
- R(round)
- S(spindle)

Casts
- G(granule)
- H(hyaline)
- W(waxy)

* : Significantly different from control at 5% level of probability
** : Significantly different from control at 1% level of probability

Table 10 Hematological findings of male rats treated orally with isocyanuric acid in the combined repeat dose and reproductive/developmental toxicity screening test

Dose (mg/kg)	No. of animals	RBC ($10^4/\mu l$)	Hb (g/dl)	Ht (%)	MCV (fl)	MCH (pg)	MCHC (%)	Ret. (%.)	WBC ($10^2/\mu l$)	Plat. ($10^4/\mu l$)	PT (sec)	APTT (sec)
0	10	805 ± 47	14.9 ± 0.4	43.7 ± 0.9	55 ± 3	18.5 ± 0.8	34.0 ± 0.4	26 ± 10	69 ± 14	133 ± 18	13.0 ± 0.3	19.4 ± 1.5
10	10	806 ± 29	14.9 ± 0.6	43.9 ± 1.3	54 ± 2	18.5 ± 0.9	33.9 ± 0.5	26 ± 7	71 ± 16	131 ± 15	13.3 ± 0.4	18.5 ± 0.6
40	10	821 ± 29	15.0 ± 0.5	44.2 ± 1.4	54 ± 2	18.3 ± 0.7	33.9 ± 0.5	23 ± 7	79 ± 34	137 ± 9	13.3 ± 0.3	19.6 ± 0.6
150	10	804 ± 28	15.0 ± 0.4	44.0 ± 1.0	55 ± 1	18.6 ± 0.3	34.0 ± 0.4	21 ± 5	59 ± 12	136 ± 9	13.2 ± 0.9	19.4 ± 1.0
600	10	752** ± 32	13.6** ± 0.5	40.5** ± 1.4	54 ± 1	18.1 ± 0.4	33.7 ± 0.5	32 ± 18	72 ± 20	147 ± 10	13.3 ± 0.2	18.9 ± 0.8

Each value is expressed as mean±S.D.
** : Significantly different from control at 1% level of probability

Table 11 Blood biochemical findings of male rats treated orally with isocyanuric acid in the combined repeat dose and reproductive/developmental toxicity screening test

Dose (mg/kg)	No. of animals	GOT (IU/l)	GPT (IU/l)	ALP (IU/l)	γ-GTP (IU/l)	T.P. (g/dl)	Alb. (g/dl)	A/G	T-Cho. (mg/dl)	T.G. (mg/dl)
0	10	57 ± 5	33 ± 5	257 ± 68	0.34 ± 0.14	6.21 ± 0.15	3.14 ± 0.12	1.03 ± 0.10	70 ± 16	73 ± 31
10	10	52 ± 4	27** ± 3	261 ± 47	0.25 ± 0.20	6.27 ± 0.24	3.20 ± 0.21	1.04 ± 0.12	83 ± 17	83 ± 40
40	10	50 ± 4	27** ± 3	240 ± 50	0.70 ± 0.78	6.33 ± 0.17	3.26 ± 0.16	1.07 ± 0.08	71 ± 10	83 ± 34
150	10	53 ± 10	28* ± 5	262 ± 57	0.50 ± 0.43	6.35 ± 0.23	3.25 ± 0.10	1.06 ± 0.07	76 ± 14	88 ± 37
600	10	55 ± 7	27** ± 5	254 ± 38	0.68* ± 0.21	6.21 ± 0.26	3.18 ± 0.14	1.05 ± 0.10	85 ± 11	69 ± 30

Dose (mg/kg)	No. of animals	Glu. (mg/dl)	T-Bil. (mg/dl)	BUN (mg/dl)	Crea. (mg/dl)	Ca (mg/dl)	P (mg/dl)	Na (mEq/l)	K (mEq/l)	Cl (mEq/l)
0	10	141 ± 14	0.30 ± 0.02	14.2 ± 2.8	0.57 ± 0.05	10.1 ± 0.3	7.3 ± 0.4	142.9 ± 0.9	4.20 ± 0.25	101 ± 1
10	10	156* ± 11	0.28 ± 0.03	13.8 ± 1.4	0.57 ± 0.05	10.2 ± 0.3	7.2 ± 0.6	142.4 ± 0.8	4.36 ± 0.22	101 ± 1
40	10	151 ± 9	0.28 ± 0.02	12.0 ± 1.0	0.57 ± 0.05	10.3 ± 0.2	7.5 ± 0.6	143.0 ± 1.1	4.13 ± 0.19	101 ± 1
150	10	155 ± 17	0.31 ± 0.03	13.3 ± 1.1	0.58 ± 0.05	10.3 ± 0.3	7.3 ± 0.7	143.2 ± 0.9	4.22 ± 0.31	101 ± 1
600	10	140 ± 6	0.29 ± 0.04	38.2** ± 12.8	1.08** ± 0.37	10.4 ± 0.2	8.5 ± 1.4	141.6* ± 1.6	4.46 ± 0.44	100 ± 1

Each value is expressed as mean±S.D.
* : Significantly different from control at 5% level of probability
** : Significantly different from control at 1% level of probability

Table 12 Incidence of necropsy findings of male rats treated orally with isocyanuric acid in the combined repeat dose and reproductive/developmental toxicity screening test

Organ : Findings	Degree	Dose(mg/kg) 0	10	40	150	600
		Fate: TK (T)	TK FP (T)	TK UC (T)	TK (T)	TK (T)
		No. of animals: 10 (10)	8 2 (10)	9 1 (10)	10 (10)	10 (10)
Liver : Diaphragmatic nodule	-	10 (10)	7 2 (9)	9 1 (10)	10 (10)	10 (10)
	+	0 (0)	1 0 (1)	0 0 (0)	0 (0)	0 (0)
Kidney : Enlargement	-	10 (10)	8 2 (10)	9 1 (10)	10 (10)	3 (3)
	+	0	0 0	0 0	0	4
	++	0)(0)	0 0)(0)	0 0)(0)	0) (0)	3)(7)**
Decoloration	-	10 (10)	8 2 (10)	9 1 (10)	10 (10)	3 (3)
	+	0	0 0	0 0	0	5
	++	0)(0)	0 0)(0)	0 0)(0)	0) (0)	2)(7)**
Adrenal : Decoloration	-	10 (10)	8 2 (10)	9 1 (10)	10 (10)	4 (4)
	+	0 (0)	0 0 (0)	0 0 (0)	0 (0)	6 (6)**
Skin : Alopecia	-	10 (10)	8 2 (10)	9 1 (10)	9 (9)	10 (10)
	+	0 (0)	0 0 (0)	0 0 (0)	1 (1)	0 (0)

- : Negative; + : Slight; ++ : Moderate; TK : Terminal kill; FP : Failed to cause pregnancy, killed at the termination;
UC : Animal with unsuccessful copulation, killed at the termination; T : Total
** : Significantly different from control at 1% level of probability

Table 13 Incidence of necropsy findings of female rats treated orally with isocyanuric acid in the combined repeat dose and reproductive/developmental toxicity screening test

Organ : Findings	Degree	Dose(mg/kg)	0	10	40	150	600
		Fate	TK (T)	TK NP (T)	TK UC KL (T)	TK KL (T)	TK (T)
		No. of animals	10 (10)	8 2 (10)	8 1 1 (10)	9 1 (10)	10 (10)
Stomach : Distention	-		10 (10)	8 2 (10)	8 1 0 (9)	9 1 (10)	10 (10)
	++		0 (0)	0 0 (0)	0 0 1 (1)	0 0 (0)	0 (0)
Kidney : Enlargement	-		10 (10)	8 2 (10)	8 1 1 (10)	9 1 (10)	0 (0)
	+		0	0 0	0 0 0	0 0	4
	++		0 (0)	0 0 (0)	0 0 0 (0)	0 0 (0)	6 (10)**
Decoloration	-		10 (10)	8 2 (10)	8 1 1 (10)	9 1 (10)	1 (1)
	+		0	0 0	0 0 0	0 0	6
	++		0 (0)	0 0 (0)	0 0 0 (0)	0 0 (0)	2 (9)**
	+++		0	0 0	0 0 0	0 0	1
Adrenal : Decoloration	-		10 (10)	8 2 (10)	8 1 0 (9)	9 0 (9)	5 (5)
	+		0	0 0	0 0 1	0 1	2
	++		0 (0)	0 0 (0)	0 0 0 (1)	0 0 (1)	3 (5)**
Thymus : Atrophy	-		9 (9)	7 2 (9)	8 1 0 (9)	9 1 (10)	6 (6)
	+		1 (1)	1 0 (1)	0 0 1 (1)	0 0 (0)	4 (4)
Skin : Alopecia	-		10 (10)	8 2 (10)	8 1 1 (10)	9 1 (10)	9 (9)
	+		0 (0)	0 0 (0)	0 0 0 (0)	0 0 (0)	1 (1)

- : Negative; + : Slight; ++ : Moderate; +++ : Marked; TK : Terminal kill; NP : Non-pregnant; UC : Animal with unsuccessful copulation; KL : Killed because all pups died after delivery; T : Total
* : Significantly different from control at 5% level of probability
** : Significantly different from control at 1% level of probability