Summary of Inhalation Carcinogenicity Study of 1-Bromobutane in F344 Rats

March 2008

Japan Bioassay Research Center

Japan Industrial Safety and Health Association

PREFACE

The tests were contracted and supported by the Ministry of Health, Labour and Welfare of Japan. The tests were conducted by Japan Bioassay Research Center (JBRC) and the report was prepared by JBRC and peer reviewed by outside expert pathologist. Complete report was submitted to Ministry of Health, Labour and Welfare of Japan on March 31, 2008.

This English Summary was translated by JBRC from Japanese complete report.

Summary of Inhalation Carcinogenicity Study of 1-Bromobutane in F344 Rats

Purpose, materials and methods

1-Bromobutane (CAS No. 109-65-9) is a colorless liquid with a boiling point of 101.3°C. It is soluble in alcohol and ether and insoluble in water.

The carcinogenicity and chronic toxicity of 1-bromobutane (greater than 99.7% pure) were examined by inhalation exposure using groups of F344/DuCrlCrlj (Fischer) rats. Each group of test animals consisted of either 50 male or 50 female rats. Test animals were exposed to 1bromobutane vapor at target concentrations of 0 (clean air), 125, 250 or 500 ppm (v/v) for 6 hours/day, 5 days/week for 2 years (104 weeks). Both sexes were exposed to each concentration of 1-bromobutane vapor. The highest dose level was chosen so as not to exceed the maximum tolerated dose (MTD), based on both growth rate and toxicity in a previous 13-week toxicity study. The identity of the 1-Bromobutane used in these experiments was confirmed by both infrared spectrometry and mass spectrometry, and it was analyzed by gas chromatography before and after its use to affirm its stability. Stainless-steel inhalation exposure chambers (volume: 8500 L) were used throughout the 2-year exposure period. 1-Bromobutane vapor-air mixtures were generated by bubbling clean air through 1-bromobutane liquid and the mixtures supplied to the inhalation exposure chambers. Air concentrations of 1-bromobutane vapor in the inhalation exposure chambers were monitored at 15 min intervals by gas chromatography. The animals were observed daily for clinical signs and mortality. Body weight and food consumption were measured once a week for the first 14 weeks and every 4 weeks thereafter. All animals, including those found dead or in a moribund state as well as those surviving to the end of the 2-year exposure period, underwent complete necropsy. Urinalysis was performed near the end of the exposure period. For hematology and blood biochemistry at the terminal necropsy, surviving animals were fasted overnight and bled under deep ether anesthesia. Organs and tissues were removed, weighed and examined for macroscopic lesions at necropsy. The organs and tissues were then fixed and embedded in paraffin. Five µm thick tissue sections were prepared and stained with hematoxylin and eosin and examined microscopically. Incidences of neoplastic lesions were statistically analyzed by Fisher's exact test. Any positive dose-response trends of 1-Bromobutane induction of neoplastic lesions were analyzed by Peto's test. Incidences of non-neoplastic lesions and urinalysis were analyzed by the Chi-square test. Changes in body weight, food consumption, hematological and blood biochemical parameters, and organ weights were analyzed by Dunnett's test. The present studies were conducted in

accordance with the Organisation for Economic Co-operation and Development (OECD) Good Laboratory Practice and with reference to the OECD Guideline for Testing of Chemicals 451 "Carcinogenicity Studies".

Results

The body weights of the highest exposure groups, 500 ppm-exposed males and females, were slightly decreased: terminal body weights of the 500 ppm-exposed males and females were suppressed to 83% and 90% of their respective controls. No other significant differences in survival rate or clinical symptoms were found between the 1-bromobutane-exposed groups of either sex and their controls.

No significant increase in the incidence of neoplastic lesions was found in any of the 1-bromobutane-exposed groups of either sex compared with their controls. There was, however, an increase in the incidence of eosinophilic change in the respiratory epithelium in males exposed to 500 ppm 1-bromobutane and an increase in the severity of eosinophilic change in the olfactory epithelium of males exposed to 250 ppm and 500 ppm 1-bromobutane.

Conclusions

There was no evidence of carcinogenic activity of 1-bromobutane in male or female rats.

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TABLE A

CONCENTRATIONS OF 1 - BROMOBUTANE IN THE INHALATION CHAMBER OF THE 2-YEAR INHALATION STUDY

CONCENTRATIONS OF 1-BROMOBUTANE IN THE INHALATION CHAMBER OF THE 2-YEAR INHALATION STUDY

Group Name	Concentration(ppm) $Mean \pm S.D.$
Control	0.0 ± 0.0
125 ppm	125.2 ± 0.4
250 ppm	250.5 ± 1.0
500 ppm	500.8 ± 1.9

TABLE D1

BODY WEIGHT CHANGES AND SURVIVAL ANIMAL NUMBERS : MALE

(BI0040)

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrICrIj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

	,	1011100		mdd cor	=		udd ncz	a		200 ppm	E .	
Week-Day on Study	Av. Wt.	No. of Surviv. <50>	Av. Wt.	% of cont. <50>	No.of Surviv.	Av. Wt.	% of cont. <50>	No. of Surviv.	Av. Wt.	% of cont. <50>	No. of Surviv.	
0-0	116 (50)	50/50	_	100	50/50	116 (50)	100	50/50	116 (50)	100	E0 /E0	
1-7	_	20/20	_	66	50/50		95	50/50	_	66	50/50	
2-7		20/20	175 (50)	66	20/20		94	50/50	159 (50)	7 G	50/50	
3-7	_	20/20	_	100	50/50		95	50/50	_	8 8	50/50	
4-7	_	20/20	_	100	50/50		94	50/50	_	8 8	50/50	
2-5	_	20/20		100	50/50	229 (50)	95	50/50	_	8 88	50/50	
2-9	256 (50)	20/20	_	100	20/20	244 (50)	95	50/50	225 (50)	8 8	50/50	
2-2		20/20		100	50/50	259 (50)	98	50/50		88	50/50	
2-8		20/20		100	20/20		96	20/20		88	50/20	
2-6		20/20		100	20/20		26	20/20		88	50/50	
10-7	304 (50)	20/20	_	100	20/20		96	20/20	_	88	50/50	
11-7		20/20		100	20/20		96	50/50	272 (50)	87	50/50	
12-7		20/20	319 (20)	100	20/20		96	50/50	277 (50)	87	50/50	
13-7		20/20		101	20/20		96	50/50	_	87	50/50	
14-7	331 (50)	20/20		101	50/50		96	20/20	_	87	50/50	
18-7	_	20/20	320 (20)	102	20/20		26	50/50	303 (20)	88	50/50	
22-7	-	20/20		102	20/20		26	50/50	_	88	50/50	
26-7	_	20/20		102	20/20		26	49/50	_	88	50/20	
30-7	385 (20)	20/20		101	20/20		26	49/50	338 (50)	88	50/50	
34-7	_	20/20		102	20/20	385 (49)	86	49/20	_	88	50/50	
38-7		20/20		102	20/20		86	49/50	_	68	50/50	
42-7	_	20/20	419 (50)	102	20/20		86	49/50	_	88	50/50	
46-7		20/20		102	20/20	407 (49)	86	49/50	_	88	50/50	
20-7	-	20/20	_	101	20/20	410 (49)	26	49/50	_	88	50/50	
54-7		20/20		101	20/20		26	49/50	371 (50)	87	50/50	
28-7	_	20/20	434 (50)	102	20/20		86	49/20	_	88	50/50	
62-7	-	20/20		101	20/20		86	49/50	_	88	50/50	
2-99	-	20/20		101	20/20		26	49/20	_	87	50/50	
7-07	_	20/20		102	49/50		26	49/50	378 (49)	87	49/50	
74-7	_	20/20	_	102	47/50	425 (49)	26	49/50	378 (49)	87	49/50	
7-87	_	49/50	_	100	46/50		96	49/20	378 (48)	82	48/50	
2-28	-	48/50	_	100	44/50		95	49/50	374 (48)	82	48/50	
2-98		48/50		100	43/50		95	49/50	373 (45)	82	45/50	
2-06		47/50		100	42/50	418 (48)	96	48/50	372 (44)	82	44/50	
94-7		46/50		100	40/20		96	46/50	364 (43)	84	43/50	
2-86	_	45/50	_	100	38/20	415 (44)	26	44/50	363 (41)	82	41/50	
102-7	_	44/50	423 (37)	102	37/20	410 (43)	66	43/50	355 (40)	98	40/50	
104-7	420 (30)	20 /EO	(35)	9	02/20	AOF (A1)	ć	(L) 11		ć		

TABLE D2

BODY WEIGHT CHANGES AND SURVIVAL ANIMAL NUMBERS : FEMALE

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : AI 104
SEX : FEMALE

PAGE: 2

E	No. of	Surviv.		50/50	50/50	50/50	50/50	50/20	50/20	20/20	50/50	50/50	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	49/50	47/50	46/50	4b/50 44/50	44/50 44/E0	44/50	44/50	42/50	38/50	37/50		
500 ppm	% of	cont.	<20>	100	92	94	93	92	92	93	93	94	92	94	94	94	96	94	92	92	92	96	96	96	26	96	96	94	92	94	95	94	94	56	# C	દે કે	3 6	06	06	06	***************************************	
	Av. Wt.			96 (50)	_		_		140 (50)												_	_	200 (50)	_	_	215 (50)		220 (50)		228 (50)	_		245 (46)	247 (46)	_	_	_	_	_		****	
EQ.	No. of	Surviv.		50/50	50/50	50/50	50/50	20/20	50/50	50/50	50/50	50/50	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	50/50	50/50	50/50	90/20	50/50	30/30	46/50	45/50	43/50	42/50	41/50	Λν Ψτ : σ	40
udd ocz	Jo %	cont.	<20>	100	97	86	26	26	26	86	66	66	66	100	100	101	101	100	102	102	100	102	102	101	102	101	102	100	101	100	100	66 6	6	8 6	600	90	- 86	97	97	96	V	;
	Av. Wt.			96 (50)	_	120 (50)	_	_	_	153 (50)	_		168 (50)				_		_	_	_	_	_	_	_	_	_		240 (50)		_	253 (50)	(22) (20)			_	_	_	_	_	ed animals	oramin po
	No. of	Surviv.		50/50	50/50	50/50	50/50	50/50	50/50	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	50/50	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	20/20	49/50	49/50	49/50	49/50	48/50	46/50	48/50	48/50	47/50	46/50	44/50	43/50	to of measur	10.01
india on the	% of	cont.	<20>	100	86	66	66	66	86	66	66	101	100	101	101	101	102	101	102	101	100	101	100	100	101	100	101	66	100	100	100	007	100	9 9	100	66	66	86	86	66	1:():	
	Av. Wt.			96 (50)	_	_	_	_		154 (50)	160 (50)		169 (50)				183 (50)						210 (50)									255 (49)	260 (46)							279 (43)	>:No. of effective animals. ():No. of measured	2000
TOTILO	No. of	Surviv.	<20>		0) 20/20) 50/50) 50/50) 50/50) 50/50) 50/50					09/20							0) 50/50								_	>:No. of eff	
	Av. Wt.			96 (50					_	_		165 (50)				178 (50)			188 (50)							225 (50)				242 (50)		(00) 667						_	_	283 (38)	~	
		Week-Day	on Study	0-0	1-7	27	3-7	4-7	22	29	L-L	2-8	2-6	10-7	11-7	7-21	13-7	14-7	18-7	1.–22	7-97	30-7	34-7	38-7	42-7	46-7	2-0-2	54-7	2-89-7	7-29	<i>)</i> 99	1-01	78-7	89-7	86-7	2-06	94-7	2-86	102-7	104-7	TO THE POPULATION OF THE POPUL	

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TABLE D3

BODY WEIGHT CHANGES: MALE

UNIT : g REPORT TYPE : A1 104 SEX : MALE												٨		H	PAGE: 1
Group Name	Admini 0-0	istration	Administration week-day 0-0		2-7		3-7	- Company of the Comp	4-7		5-7		2-9		
Control	+ 911	٧	- VVI	•	- t										
10131100	-011	Þ	144-	ø	H / / T	ה	∓203	ກ	7.55 +	10	$241\pm$	11	256±	11	
125 ppm	116±	9	142±	ø.	175 =	10	$202\pm$	10	224±	10	242±	12	257±	13	
250 ppm	116±	9	137±	**	167±	10**	192±	#	212±	12**	229 ±	13**	244±	13**	
500 ppm	116±	9	132±	**	159±	**	179±	** 6	198±	10**	213±	10**	225 ±	 	
Significant difference .	V Q	- OF	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	,			E								
organitations difference ;		60.7	ĭo .				Test of Dunnett	unnett							

Tough Name Administration Week-day 9-7 $10-7$ $11-7$ $11-7$ $12-7$ $13-7$	UNIT : g REPORT TYPE : AI 104 SEX : MALE														PA	PAGE:
$272\pm 12 \qquad 284\pm 12 \qquad 294\pm 13 \qquad 304\pm 14 \qquad 312\pm 15 \qquad 318\pm 16 \qquad 325\pm 14 \qquad 305\pm 14 \qquad 305\pm 15 \qquad 313\pm 15 \qquad 319\pm 15 \qquad 328\pm 15 \qquad 319\pm 15 \qquad 328\pm 15 \qquad 313\pm 15 \qquad 319\pm 15 \qquad 328\pm 15 \qquad 328\pm 15 \qquad 313\pm 15 \qquad 319\pm 15 \qquad 328\pm 15 \qquad 328\pm$	Group Name	Admin 7-7	nistration 7	week-day	***************************************	7-0		7-01		11 7					Aller over	
$272\pm 12 \qquad 284\pm 12 \qquad 294\pm 13 \qquad 304\pm 14 \qquad 312\pm 15 \qquad 318\pm 16 \qquad 318\pm 16 \qquad 325\pm 328\pm 14 \qquad 305\pm 14 \qquad 305\pm 15 \qquad 313\pm 15 \qquad 319\pm 15 \qquad 328\pm 328\pm 328\pm 328\pm 328\pm 328\pm 328\pm 328\pm$				-		6		101		111-(12–2	-0000000000	13-7	TO COMPANY OF THE PARTY OF THE	
$272\pm 14 + 285\pm 14 + 295\pm 14 + 305\pm 15 + 4 + 305\pm 15 + 4 + 305\pm 15 + 4 + 301\pm 17 + 4 + 306\pm 17 + 4 + 301\pm 17 + 4 + 301\pm 17 + 4 + 301\pm 17 + 4 + 313\pm 13 + 313\pm 12 + 4 + 250\pm 13 + 4 + 260\pm 14 + 267\pm 14 + 267\pm 14 + 272\pm 14 + 277\pm 15 + 283\pm 12 + 1285\pm 12 + $	Control	272±			~	294±	13	304±	14	312±	15	318±	16	325±	17	
$259\pm 14** \qquad 272\pm 15** \qquad 284\pm 16** \qquad 292\pm 16** \qquad 301\pm 17** \qquad 306\pm 17** \qquad 313\pm 238\pm 12** \qquad 250\pm 13** \qquad 260\pm 14** \qquad 267\pm 14** \qquad 277\pm 14** \qquad 277\pm 15** \qquad 283\pm 283\pm 12** \qquad 283\pm 12** \qquad 280\pm 1$	125 ppm	272			₩.	295±	14	305±	15	313±	15	319+	15	328±	16	
$238\pm$ $12**$ $250\pm$ $13**$ $260\pm$ $14**$ $267\pm$ $14**$ $277\pm$ $14**$ $277\pm$ $15**$ $283\pm$ *: $P \le 0.05$ **: $P \le 0.05$ **: $P \le 0.01$	250 ppm	559±			*	284±	I6**	292±	16**	301∓	17**	306±	17**	313±	17**	
*: P ≤ 0.05 **: P ≤ 0.01	900 ppm	238±			*	760 ±	14**	267±	14**	272±	14**	277±	15**	283±	15**	
*: P ≤ 0.05 **: P ≤ 0.01																
	Significant difference;		0.05	** : P ≤ 0.01				Test of D	nnett	OCCUPATION OF THE PROPERTY OF						

ANIMAL : RAT F344/Ducricrij[F344/Ducrj] UNIT : g REPORT TYPE : Al 104 SEX : MALE	j[F344/DuCr.j]			•	DOUL WELCHI CHANGES ALL ANIMALS	CHANGES	(SUMMAKY)								PAGE: 3
Group Name	Adminis	tration	Administration week-day										Addition of the second		
0.1	14-1		18-7		22-7		26-7	MATERIAL STATE OF THE STATE OF	30-7	000000000000000000000000000000000000000	34-7		38-7		
Control	331+	17	343.±	18	362±	18	377±	18	385±	20	393+	20	400∓	. 22	
125 ppm	334±	16	350±	17	∓69€	19	383+	21	390±	21	400 ∓	22	409 +	. 24	
250 ppm	318+	18##	333±	18**	352±	19*	∓99€	18*	374±	18*	385±	20	393+	61 :	
500 ppm	+1 888 7	15**	303∓	16**	317±	18**	332+	19**	338+	20**	347±	21**	355±	: 22**	
Significant difference ;	*: P ≤ 0.05		* : P ≤ 0.01		- Apply Apply and Appl		Test of Dunnett	unnett			Military and the second				
(HAN260)	- 0.0 A W. M.		Visit Annual Control				TO CONTRACTOR OF THE PARTY OF T	10000000000000000000000000000000000000	-						BAIS 4

ANIMAL : RAT F344/DucrlCrlj[F344/DuCrj] UNIT : g REPORT TYPE : Al 104 SEX : MALE	j[F344/DuCrj]			ALL	ANIMALS	ALL ANIMALS	(SUMMAKY)							PAGE :
Group Name	Adminis 42-7	stration	Administration week-day 42-7 46-7	TY / Y W Over	50-7		54-7		58-7		62-7		2-99	
Control	410±	22	416±	23	421±	23	426±	24	427±	24	431±	24	434±	26
125 ppm	419±	26	423±	27	427±	28	431±	28	434±	30	437±	30	440 ±	30
250 ppm	$401\pm$	20	407±	19	410±	20	414±	22	418±	21	422±	23	421±	22*
500 ppm	361±	23**	∓99€	24**	370±	24**	371±	23*≠	375±	23**	381+	24**	378±	23**
Significant difference ;	* : P ≤ 0.05		**: P \leq 0.01	1	75 Account		Test of Dunnett	unnett	***************************************	and the second s		- Valenting and the state of th	700000000000000000000000000000000000000	

Group Name Administration week-day 78-7 78-7 85-7 86-7 90-7 Control 433± 37 436± 39 443± 25 442± 26 440± 27 437± 2 125 ppm 443± 29 444± 30 443± 30 442± 32 441± 31 439± 3 250 ppm 422± 23** 425± 24** 425± 24** 425± 24** 422± 28** 419± 31** 418± 2 500 ppm 378± 23** 378± 24** 378± 22** 372± 2 2	UNIT : g REPORT TYPE : AI 104 SEX : MALE														PAG	PAGE :
433± 37 436± 39 443± 25 442± 26 440± 27 437± 443± 39 443± 30 442± 32 441± 31 439± 422± 23** 425± 24* 425± 24** 425± 24** 419± 31** 418± 378± 23** 378± 24** 378± 22** 374± 26** 373± 29** 372±	oup Name	Admin. 70-7	istration	week-day		7-87		82-7	TRANSPORTATION OF THE PROPERTY	2-98		2-06		94-7	***	
443± 29 444± 30 443± 30 442± 32 441± 31 439± 422± 23** 425± 24** 425± 24** 422± 28** 419± 31** 418± 378± 23** 378± 24** 378± 22** 374± 26** 373± 29** 372±	Control	433±			6	443±	25	442±	26	440±	27	437±	27	432 ±	31	
422± 23** 425± 24* 425± 24** 422± 28** 419± 31** 418± 378± 23** 378± 22** 378± 29** 372±	125 ppm	443±	59		0	443±	30	442±	32	441 ±	31	439∓	33	430=	35	
378± 23** 378± 24** 378± 22** 374± 26** 373± 29** 372±	250 ppm	422±	23**		4 *	425±	24**	422±	28**	419±	31**	418±	29**	414=	28 *	
	500 ppm	378±			4 * ★		22**	374±	26**	373±	29**	372±	2 4**	364±	29 **	
Significant difference ; *: P ≤ 0.05 **: P ≤ 0.01 Test of Dunnett	Significant difference ;	VI		# : P ≤ 0.01				Test of Du	unett			A00-1		- Charles of the Control		

PAGE: 6						BAIS 4
(SUMMARY)						Test of Dunnett
CHANGES		32	30	26	29* ∗	
BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS	104-7	420±	417±	405±	350∓	
		44	30	27	29 **	01
	Administration week-day 98-7 102-7	414±	423±	410±	355 ±	* : P ≤ 0.01
[j	nistratic 7	32	32	26	25**	0.05
21j[F344/DuCr.	Admir 98-7	428 ±	429 ±	415±	∓898	P 00 09
STUDY NO.: 0560 ANIMAL: RAT F344/DuCrICrlj[F344/DuCrj] UNIT: g REPORT TYPE: A1 104 SEX: MALE	Group Name	Control	125 ppm	250 ppm	500 ppm	Significant difference ; (HAN260)

TABLE D4

BODY WEIGHT CHANGES: FEMALE

NUML 1 1 1 1 1 1 1 1 1
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ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	j[F344/DuCr.j]			¥	ALL ANIMALS									PAC	PAGE: 8
Group Name	Adminis: 7-7	Administration week-day.	week-day 8-7		2-6		10-7		11-7		12-7		13-7		
Control	162±	∞	165 ±	6	+ 691	σ	173+	5	177+	o	120+	C	100	c	WAS TO SERVICE OF THE
125 ppm	160+	æ	166±	, o	169	o o	174		+ 621	n o	180+	n ⊂	183 +	D C	
250 ppm	160+	6	164±	6	168±	6	173±	ა თ	177	. 01	180 + 180	a 01	182 +	10	
200 mid 005	150±	**9	155±	/**	160±	7**	163±	*	167±	* * &	±89I	** &	172±	**	
Significant difference;	* : P ≤ 0.05		* : P ≤ 0.01),1	**************************************	* ************************************	Test of Dunnett	unnett				Mary last and the second		, —	

STUDY NO. : 0560 ANUMAL : RAT F344/DuCr.LCr.Lj[F344/DuCr.j] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	[F344/DuCr.j.]		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)			PAG	PAGE: 9
Group Name	Administration week-day_ 14-7	n week-day 18-7	7-22	26-7	30-7	. 34-7	38-7	
Control	183± 10	188± 10	195土 11	201± 12	204± 12	209± 13	215± 14	
125 ppm	185± 10	191 10	197± 12	202± 11	206± 12	210± 13	216± 13	
250 ppm	183± 11	191± 11	198± 12	202 ± 13	208± 12	214± 13	218± 14	
500 ppm	172± 8**	179± 8	8** 186± 9**	190 ∓ 10*	195± 10**	200± 10**	206± 10**	
Significant difference ;	*: P 6.05	** : P ≤ 0.01		Test of Dunnett				

PAGE: 10	770000000	The state of the s	22	19	24	14**	
	2-99	and an analysis of the state of	249 ±	250±	250±	236±	
	771000000	V0000	21	17	21	13**	
	62-7		242±	242±	242±	228+	
			19	17	21	13**	
	58-7		238±	237 ±	240±	225±	
			17	16	19	1 <u>1</u> *	nnett
(SUMMARY)	54-7		235±	233±	236±	220±	Test of Dunnett
CHANGES			16	16	17	11**	***************************************
BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS	50-7		228±	530±	233±	219±	
		NAME OF THE PARTY	15	14	17	11*	01
	Administration week-day 42-7	WATER TO THE PARTY OF THE PARTY	225 ±	224±	728 ±	215±	** : P ≤ 0.01
Ĺĵ	nistrati 7		14	14	16	11*	0.05
-1 j [F344/DuCr.	Admini: 42-7		221±	223±	726±	214±	* P S
STUDY NO.: 0560 ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	Group Name	MATERIAL STATE OF THE STATE OF	Control	125 ppm	250 ррш	ლშშ 200	Significant difference; *: P ≤ 0.05

(HAN260)

BAIS 4

STUDY NO. : 0560 ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	j[F344/DuCrj]			BODY ₩ ALL ANI.	EIGHT C	HANGES	BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS							PAG	PAGE: 11
Group Name	Administr 70-7	Administration week-day_70-7	ay 74-7		7-87	TO A PACE.	82-7		2-98		2-06		94-7		
Control	255± 23		261± 22		∓997	26	∓697	32	273±	32	279±	36	277±	23	
125 ppm	255± 21		260± 21	-,	765±	21	270±	22	273±	23	275±	23	275±	25	
250 ppm	253± 25		259± 26	- 1	261±	27	792∓	24	792 7	27	270±	26	271±	53	
500 рри	240# 14	14**	245± 14**		247 ==	17**	253±	16*≠	255±	18**	257±	19**	728 ±	23**	
Significant difference ;	*: P ≤ 0.05	5 *‡: P ≤ 0.01	≤ 0.01	North Address of the Control		***************************************	Test of Dunnett	unnett							000000000000000000000000000000000000000
(HAN260)									77 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	Managadoo.		200		A production of the format of	BAIS 4

STUDY NO. : 0560 ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	j [F344/DuCr.j.]		BODY ALL AI	BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)
Group Name	Administrati	noi-doow doi		and should be a second of the	
The state of the s	88-7	98-7		104-7	
			- Principal Prin	TOTAL	
Control	283± 23	284± 2	22	283± 23	
125 ppm	277± 27	279 ± 2	25	279± 24	
250 ppm	274± 27	276± 2	28	273± 28	
500 ppm	256± 24**	729	22**	254± 22**	
	The state of the s	A Annah di A			
Significant difference ;	* : P ≤ 0.05	**: P ≤ 0.01			Test of Dunnett
(HAN260)			P. Carrier Communication Commu	1000	BAIS 4

TABLE E1

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL

NUMBERS: MALE

(BI0040)

MEAN FOOD CONSUMPTION (FC) AND SURVIVAL

PAGE :					A CONTRACTOR OF THE CONTRACTOR																														
500 ppm	**************************************	% of No. of	cont. Surviv.		82 50/50			102 50/50 106 50/50			106 50/50					114 50/50					116 50/50					112 50/50								[0] 43/50	
50		Av. FC. %	00)C\	(20)	(20)	15.6 (50)	(20)	(20)	(20)	(20)	(20)	(20)	(50)	(50)	18.5 (50) 11	(20)	(20)	(20)		(20)	(20)	(20)	(20)	(20)	19.1 (50) 11	(20)	(49)	(49)	(48)	(48)	(42)	(44)	16.9 (43) 10	(40)
250 ppm			cont. Surviv.			95 50/50	97 50/50								105 50/50	105 50/50					105 49/50				104 49/50	104 49/50 102 40/50		102 49/50				102 49/50		99 46/50	
10000000		Av. FC.		- Translated	12.3 (50)		16.0 (50)	17.2 (50)			17.1 (50)			17.4 (50)		17.1 (50)	17. 2 (50)				16.9 (49)	16.9 (49)				16.7 (49)		_		_	_		_	16.6 (46) 16.7 (44)	
125 ppm			Surviv.		20/20	50/50	50/50	50/50	20/20	20/20	20/20	20/20	20/20	50/50	90/20	50/50	50/50	50/50	20/20	50/50	50/50	50/50	20/20	20/20	50/50	50/50	50/50	49/50	47/50	46/50	44/50	43/50	42/50	40/50 38/50	99/ 50 97 /E0
125		Av. FC. % of	cont. <50>		13.0 (50) 95	(50)	(20)	(20)	(20)	(20)	(20)	(20)	(20)	17.4 (50) 106	(00)	(50)		(20)		(20)	16.8 (50) 104 17 1 (50) 106	(20)	(20)	(20)		16 9 (50) 104	(20)	(49)	(47)	_	(44)	(43)	17. 1 (42) 101		
Control		Av. FC. No. of	out viv. (50)		(20)	15.5 (50) 50/50 16 F (E0) E0/E0	(20)	(20)	(20)	(20)	(20)	_	(20)	16.4 (45) 50/50 16.3 (50) 50/50	(20)		(20)	(20)	(20)		_	(20)	(20)	(20)	16.5 (50) 50/50		(20)	(20)	2 (20)	4 (49)	(48)	(48)	16.0 (47) 47/50		3
1000 and 100		Woob-Day	on Study		1-7	2- <i>f</i> 3-7	4-7	5-7	2-9	7-7	8-7	7-6	10-7	11-7	13-7	14-7	18-7	22-7	26-7	30-7 34 7	38-7	42-7	46-7	50-7	54-7	58-1 62-7	2-99	7-07	74-7	78-7	82-7	2-98	90-7	7-86	109-7

TABLE E2

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL

NUMBERS: FEMALE

(BI0040)

MEAN FOOD CONSUMPTION (FC) AND SURVIVAL

2

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCr]]
UNIT : 8
REPORT TYPE : A1 104
SEX : FEMALE

							k				1	
Week-Day	Av. FC.	No. of Surviv.	Av. FC.	% of cont.	No. of Surviv.	Av. FC.	% of cont.	No. of Surviv.	Av. FC.	% of cont.	No. of Surviv.	
)			(00)			<90<		
1-7	10.3 (50)	02/09	i	86	20/20	1	93	50/50	9.0 (50)	87	50/50	TOO
2-7				102	20/20		86	20/20	_	26	50/50	
3-7	11.1 (50)	-		103	20/20		102	20/20		66	50/50	
4-7	_			104	20/20	11.5 (50)	106	20/20	_	103	50/50	
2-2	_			103	50/50		109	20/20	_	106	50/50	
2-9	10.5 (50)			105	50/50	4	109	50/50	11, 7 (50)	: II	50/50	
2-7	_			105	20/20		110	20/20	_	111	50/50	
2-8	10.4 (50)	20/20		103	20/20		105	20/20	_	109	50/50	
2-6	_		11.2 (50)	107	20/20	11.8 (50)	112	50/50	_	115	50/50	
102				107	20/20	11.5 (50)	112	50/50	_	118	50/50	
11-7	10.6 (50)	20/20		108	50/50	12.1 (50)	114	50/50	_	119	50/50	
12-7				111	20/20	m	117	50/50	_	123	20/20	
13-7		20/20		108	20/20	11.7 (50)	111	50/50	_	123	50/50	
14-7				106	20/20	11.3 (50)	107	50/50	_	117	50/50	
18-7				107	20/20		111	20/20	_	128	50/50	
22-7	10.4 (50)		10.9 (50)	105	20/20	11.7 (50)	113	20/20	13.2 (50)	127	50/50	
26-7				66	20/20		66	20/20	_	109	50/50	
30-7				108	20/20		113	20/20	_	130	50/50	
34-7				104	20/20		113	50/50	12.8 (50)	121	50/50	
38-7	11.0 (50)	50/50		103	20/20		110	20/20	_	124	50/50	
724				104	20/20	12.2 (50)	113	20/20	_	126	50/50	
46-7				86	20/20		105	20/20	_	113	50/50	
507		20/20	9	105	20/20	12.4 (50)	113	20/20	_	125	50/50	
54-7				101	20/20		106	20/20	_	118	50/50	
58-7		20/20		103	49/20		108	20/20	-	121	50/50	
62-7				105	49/20	11.9 (50)	107	20/20	12.8 (50)	115	50/50	
2-99				106	49/20		110	50/50	_	119	49/50	
20-7	11.8 (50)		6	101	49/50	12.3 (50)	104	20/20	13.4 (47)	114	47/50	
74-7	7		12.0 (48)	103	48/50		106	50/50	13.1 (46)	112	46/50	
78-7	11.5 (49)			103	48/50		102	50/50	12.5 (46)	109	46/50	
82-7			11.9 (48)	103	48/50	12.4 (50)	108	20/20	13.3 (44)	116	44/50	
2-98	_			105	48/50	11.9 (47)	105	47/50	12.8 (44)	113	44/50	
2-06	12.6 (44)		~	26	48/50	00	102	46/50	_	107	44/50	
947	12. 1 (43)		2	101	47/50	2	105	45/50	13.1 (44)	108	44/50	
2-86	7		2	96	46/50	12.3 (43)	26	43/50	12.7 (42)	100	42/50	
1027	4	-	12.5 (44)	101	44/50	12.6 (42)	102	42/50	_	105	38/50	
047	12.4 (38)	38/50	19 1 (43)	00	12/50	19 9 (41)	00	41/50		101	07/20	

TABLE E3

FOOD CONSUMPTION CHANGES: MALE

SEX : MALE		**************************************	1440000				PAGE:
Group Name	Administration 1-7(6)	Administration week-day(effective)	3-7(7)	4-7(7)	5-7(7)	(2) 2-9	7-7(7)
Control	13.7± 0.8	15.5± 0.9	16.5± 1.1	16.3± 1.1	16.3± 0.9	16.0 ± 0.9	16.5± 0.8
125 ppm	13.0± 0.9**	15.7± 1.2	16.7± 1.0	17.2± 1.2₩	17.2± 1.3**	17.0± 1.3**	17.6± 1.3**
250 ppm	12.3 1.0**	14.7± 1.3**	16.0± 1.5	16.7 ± 1.5	17.2± 1.6**	17.2± 1.5**	17.7± 1.4**
500 ppm	11.2± 0.8**	13.9± 1.2**	15.6± 1.3★	16.7± 1.3	17.3± 1.4**	17.4± 1.3*	17.9± 1.3**
Significant difference;	* : P ≤ 0.05	**: P ≤ 0.01		Test of Dunnatt			

REPORT TYPE : A1 104 SEX : MALE							PAGE
Group Name	Administration 8-7(7)	Administration week-day(effective) $8-7(7)$	10-7(7)	11-7(7)	12-7(7)	13-7(7)	14-7 (7)
Control	16.4± 0.9	16.6± 0.9	16.2± 1.1	16.4± 1.1	16.3± 1.1	16.2± 1.0	16.2± 1.0
125 ppm	17.0± 1.2**	17.3± 1.1**	16.9± 1.1*	17.4± 1.2**	17.2± 1.2**	17.3± 1.1**	17.0± 1.1**
250 ppm	17.1± 1.4**	17.5± 1.5**	17.0 ± 1.3**	17.4± 1.5**	17.1± 1.5**	17.1± 1.4**	17.0± 1.4**
200 ppm	17.4± 1.4**	18.2± 1.4**	18.3± 1.5**	18.4 ± 1.5**	18.4± 1.5**	18.5± 1.4**	18.5± 1.5**
Significant difference ;	* : P ≤ 0.05	# : P S 0.01		Test of Dunnett	T P COTONO AND		

OTODIACE: COOO ANIMAL: RAT F344/DuCrICrIj[F344/DuCrj] UNIT: B REPORT TYPE: AI 104 SEX: MALE	ij [F344/DuCr.j.]		FOUD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS	JES (SUMMARY)			PAC	PAGE:
Group Name	Administratio	Administration week-day(effective)		T T T T T T T T T T T T T T T T T T T		7777-0410	The state of the s	
The state of the s	18-7(7)	22-7(7)	26-7(7)	30-7(7)	34-7(7)	38-7(7)	42-7(7)	
			THE PART OF THE PA	WHAT BOTT THE TOTAL TOTA	WEIGHT OF THE PROPERTY OF THE		THE CONTRACT OF THE CONTRACT O	
Control	16.2 ± 1.1	16.2 ± 0.9	16.2 ± 0.9	16.2 ± 1.0	16.1± 0.9	16.1± 0.9	16.5± 0.8	
125 ppm	17.4± 1.4**	17.2± 1.4**	16.6± 1.3	17.2± 1.2*	16.8± 1.1**	17.1± 1.0**	17.0± 1.1**	
250 ppm	17.2± 1.5**	17.0 ± 1.3**	16.6± 0.9	17.2± 0.9*	16.9± 0.9**	17.2± 1.1**	16.9± 0.9*	
500 ppm	19.3± 1.9**	18.9± 1.9**	17.9± 1.7**	19.0± 1.8≠	18.6± 1.9**	18.9± 2.0**	18.5± 2.0**	
Significant difference ;	*: P ≤ 0.05	*#: P ≤ 0.01		Test of Dunnett	T. MANAGER ST.	A STANDARD CONTRACTOR OF THE STANDARD CONTRACTOR		

STORT NO. : 0.000 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] UNIT : g REPORT TYPE : A1 104 SEX : MALE	[j[F344/DuCr.j]		FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANTMALS	FES (SUMMARY)			PAG	PAGE:
Group Name	Administration 46-7(7)	Administration week-day(effective).	54-7(7)	58-7(7)	69-7(7)	(4) 4-33	(1) 11 (1)	THE PERSON NAMED IN COLUMN 1
	- The second sec				()))_70	(/)/_99	(1) 1-0)	
Contro]	16.1± 0.7	16.5± 0.8	16.5± 0.9	17.0± 0.9	16.6± 1.0	16.7 ± 0.9	16.8± 1.2	
125 ppm	16.8± 1.2**	17.1± 1.2**	16.9± 1.2	17.6± 1.3**	16.9 ± 1.1	17.6± 1.1**	17.6± 1.1**	
250 ppm	16.7± 1.0*	17.2± 0.9**	17.1± 1.1**	17.7± 1.0**	16.9± 1.2	17.2± 1.2	17.1 ± 1.0	
500 ppm	18.2± 1.8**	18.6± 1.8**	18.4± 1.7**	19.1± 2.1**	17.7± 1.6**	18.2 ± 2.1**	18.1± 2.0**	
Significant difference;	* : P ≤ 0.05	* : P ≤ 0.01		Test of Dunnett	1 1 1 m/s.		A PROCESSION AND A PROC	

REPORT TYPE : A1 104 SEX : MALE							PAGE
Group Name	Administration 74-7(7)	Administration week-day(effective)	82-7(7)	(2) 1–98	(2) 2-06	94-7(7)	(2) 2–86
Control	16.5± 1.1	16.4± 1.0	16.4 ± 1.2	16.3± 2.1	17.0± 1.4	16.8± 2.0	17.0± 1.6
125 ppm	17.2± 1.1**	16.7 ± 1.2	16.8± 1.3	16.8± 1.1	17.1± 1.6	16.8± 2.0	17.0 ± 1.4
250 թբա	17.1± 1.2	16.9± 1.6	16.7± 1.3	16.6± 1.8	17.0± 1.7	16.6± 1.9	16.7± 1.3
500 ppm	17.9± 2.0**	17.3± 1.8	17.3± 2.7*	16.8± 3.0	17.1± 2.1	16.9± 2.6	17.2± 2.2
			V.				
Significant difference ;	*: P ≤ 0.05	‡ : P ≤ 0.01		Test of Dunnett			

ANUMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] UNIT : g REPORT TYPE : A1 104 SEX : MALE Group Name

TABLE E4

FOOD CONSUMPTION CHANGES: FEMALE

STUDY NO. : 0560 ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj] UNIT : g FRPORT TYPE : A1 104 SFX : FFMAIF : A1 104	[j[F344/DuCrj]	ri ∢	FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS	GES (SUMMARY)				
Group Name	Administra	\		PARTIE AND ADDRESS OF THE PARTIES OF		1 1 1 1 1 1	PAGE :	
Ombi Asono	1-7(6)	1-7(6) 2-7(7)	3-7(7)	4-7(7)	9-7(7)	(2) 2-9	7-7 (7)	
Control	10.3± 0.8	10.9± 0.8	11.1± 0.8	10.9± 0.7	11.1± 0.9	10.5± 0.7	10.7 ± 0.8	
125 ppm	10.1± 0.7	11.1± 0.9	11.4± 0.8	11.3± 0.9	11.4± 0.8	11.0± 0.9*	11.2± 0.8*	
250 ppm	9.6± 0.8**	10.7± 0.8	11.3± 0.9	11.5± 1.0**	12.1± 1.0++	11.4± 0.9**	11.8± 1.0**	
500 ppm	9.0 ± 0.5**	10.6± 0.6	11.0± 0.7	11.2±. 0.7	11.8± 0.7**	11.7± 0.9**	11.9± 1.0**	
Significant difference;	*:P≦0.05	★:P≤0.01		Test of Dunnett				

(HAN260)

UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	. KAI F344/DUCEICFI][F344/DUCEJ] : g PE : AI 104 ALE	AL	ALL ANTMALS	COUNTRY (PAGE :
Group Name	Administration 8-7(7)	Administration week-day(effective) 8-7(7) 9-7(7)	10-7(7)	11-7 (7)	12-7 (7)	13-7(7)	14-7 (7)
Control	10.4 ± 0.9	10.5± 1.0	10.3± 0.8	10.6± 0.7	10.1± 0.7	10.5± 0.7	10.6± 0.8
125 ppm	10.7 ± 1.0	11.2± 1.1**	11.0± 0.8**	11.5± 0.9**	11.2± 1.0**	11.3± 1.2**	11.2± 1.0**
250 ppm	10.9± 0.8*	11.8± 1.1**	11.5± 0.9**	12.1± 1.0**	11.8± 1.0**	11.7± 1.0**	11.3± 0.9**
500 ppm	11.3 + 0.9**	12.1± 0.8**	12.2± 0.9★	12.6± 0.9**	12.4± 1.0**	12.9± 1.0**	12.4± 1.0**
Significant difference;	*: P ≤ 0.05	* : P ≤ 0.01		Test of Dunnett	AMARIA A A ANALAS A	The state of the s	- The state of the

ANIMAL : KAI F344/DuCrīCrīj[F344/DuCrīj] UNIT : g REPORT TYPE : AI 104 SEX : FEMALE	j[F3 4 4/DuCr.j]		ALL ANIMALS				PAG	PAGE:
Group Name	Administration 18-7(7)	Administration week-day(effective)_ 18-7(7) 22-7(7)	26-7(7)	30-7(7)	34-7(7)	38-7 (7)	42-7(7)	
Control	10.6± 0.9	10.4± 0.9	10.6± 0.8	10.3± 1.0	10.6± 0.8	11.0± 1.0	10.8± 0.9	
125 ppm	11.3± 1.1**	10.9士 1.0	10.5± 0.8	11.1± 1.1**	11.0± 1.1	11.3± 1.0	11.2 ± 1.0	
250 ррш	11.8± 1.1**	11.7土 1.0**	10.5± 0.7	11.6± 0.7**	12.0± 1.0**	12.1± 1.2**	12.2± 1.2**	
500 ppm	13.6± 1.2**	13.2± 1.2**	11.6± 1.0*	13.4± 1.4××	12.8± 1.1**	13.6± 1.3**	13.6± 1.5**	
		TO A STATE OF THE						
Significant difference ;	*: P ≤ 0.05	★ : P ≤ 0.01		Test of Dunnett	e			
(HAN260)		and discount of the contract o	TO BESTATION TO COMPANY TO THE TOTAL PROPERTY OF THE TOTAL PROPERT	- POPPER MANAGEMENT AND	The state of the s			BAIS 4

SEX : FEMALE							PAGE: 10
Group Name	Administration 46-7(7)	Administration week-day(effective) 46-7(7)	54-7(7)	58-7(7)	(2) 2-29	(2) 2-99	70-7(7)
Control	11.3± 0.9	11.0± 1.1	11.4± 1.1	11.6± 1.0	11.1± 1.0	11.4± 1.0	11.8± 0.8
125 ppm	11.1 ± 0.9	11.6± 1.1*	11.5± 1.0	11.9 ± 1.0	11.6± 1.0	12.1± 1.1**	11.9± 1.0
250 թբա	11.9± 1.3	12.4± 0.9**	12.1 ± 1.2**	12.5± 1.1*	11.9± 1.0**	12.5± 1.1**	12.3± 1.1
mdd 009	12.8± 1.3**	13.8± 1.3**	13.4± 1.2**	14.0± 1.8**	12.8± 0.9**	13.6± 1.3**	13.4± 1.1**
Significant difference .	\ \ \ \ \ \ \ \ \ \ \	; ;					

SEX : FEMALE	A WAR AND A STATE OF THE STATE	e principalis	The second secon	THE PARTY OF THE P	THE RESIDENCE OF THE PROPERTY	e deletation de la constantina della constantina	PAGE: 11
Group Name	Administration 74-7(7)	Administration week-day(effective)	82-7(7)	(2) 2-98	(1) 1-06	94–7 (7)	(1) 1–86
Control	11.7± 1.1	11.5± 1.2	11.5± 1.2	11.3± 1.3	12.6± 1.0	12.1± 1.4	12.7± 1.3
125 ppm	12.0± 1.0	11.8± 0.9	11.9± 1.1	11.9± 1.2*	12.2± 1.3	12.2 ± 1.2	12.2± 1.8
250 ppm	12.4± 1.0**	11.7± 1.0	12.4± 1.0**	11.9± 1.1*	12.8± 1.1	12.7± 1.2	12.3± 1.1
500 ррш	13.1± 1.1**	12.5± 1.7**	13.3± 1.0**	12.8± 1.1**	13.5± 1.0**	13.1± 1.3**	12.7± 1.9
		1.00(00)			And the state of t		
Significant difference;	*: P ≤ 0.05	**: P ≤ 0.01		Test of Dunnett			

Administration week-day(effective) 102-7(7) 12.4± 1.0 12.4± 1.3 12.5± 1.2 12.1± 1.3 12.6± 1.2 13.0± 0.9 13.0± 1.0	The second secon			
12.4 \pm 1.0 12.4 \pm 1.3 12.5 \pm 1.2 12.1 \pm 1.3 12.6 \pm 1.2 12.2 \pm 1.2 13.0 \pm 0.9 13.0 \pm 1.0	oup Name	Administratio 102-7(7)	on week-day(effective)	
12.5± 1.2 12.1± 1.3 12.6± 1.2 12.2± 1.2 13.0± 0.9 13.0± 1.0	Control	12.4± 1.0	12.4± 1.3	
12.6 \pm 1.2 12.2 \pm 1.2 13.0 \pm 0.9 13.0 \pm 1.0	125 ppm		12.1± 1.3	
13.0± 0.9 13.0± 1.0	250 ppm			
	200 ppm		13.0± 1.0	
	Significant difference .	V . *	5 0 0 0 0 0	

TABLE F1

HEMATOLOGY: MALE

SEX : MALE	REPORT TYPE : A1	PE : A1													PAGE:	-
Group Name NO.	NO. of Animals	RED BLOOD 1 O ⁶ / με	RED BLOOD CELL 1 O⁵∕µl	HEMOGLOBIN g / d2	BIN	HEMATOCRIT %	ЖІТ	MCV f &		MCH P &		MCHC g / d2		PLATELET 1 0³/µl	1	•
Control 3	38	8.13±	1.50	14.3+	2.8	39.5±	6.6	48.8±	2.8	17.5±	1.2	35.9±	1.7	811±	248	
125 ppm 3	34	9.10±	1.22*	15.8±	2.0*	43.3+	5.1*	47.7±	1.7*	17.4±	0.6	36.5±	8.0	813±	119	
250 ppm 4	41	8.96士	1.50*	15.5土	2.3	42.3±	5.7	47.7±	3.9**	17.4±	1.0	36.5±	1.2	834±	225	
500 ppm 3	37	9.26±	1.60**	15.5	8 8	42.8±	6.7	46.4±	2. 2**	16.8±	0.8**	36.1±	1.6	∓906	202**	
Significant difference;	1	. P ≤ 0.05		VI 0 0 1				Tact of Durnatt	++04							

SEX: MALE REPORT TYPE: A1 PAGE: 2 Group Name No. of Animals RETITIOLOCYTE PAGE: 3 Control 38 4.3 ± 3.8 ± PAGE: 3 125 ppm 34 2.9 ± 2.5 ± 500 ppm 37 3.4 ± 3.6 ± Significant difference: * : P ≤ 0.05 ** : P ≤ 0.01 Test of Dunett	SIUDY NO. : 0560 ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj] MEASURE: TIME : 1	344/DuCr1Cr1	[j[F344/DuCrj]	HEMATOLOGY (SUMMARY) ALL ANIMALS (105W)	
NO. of Animals RETICULOCYTE Animals % Animals % (trol 38 4.3± 3.8) ppm 34 2.9± 2.5*) ppm 41 3.9± 6.2**) ppm 37 3.4± 3.6** cant difference: *: P ≤ 0.05 **: P ≤ 0.01 Test of Dumett	SEX : MALE		TYPE : A1		PAGE: 2
Control 38 4.3± 3.8 125 ppm 34 2.9± 2.5* 250 ppm 41 3.9± 6.2** 500 ppm 37 3.4± 3.6** ificant difference; *: P ≤ 0.05 **: P ≤ 0.01 Test of Dunett	Group Name	NO. of Animals	RETICULOCYTE %		
125 ppm 34 2.9± 2.5* 250 ppm 41 3.9± 6.2** 500 ppm 37 3.4± 3.6** ificant difference; *:P ≤ 0.05 **:P ≤ 0.01 Test of Dunnett	Control	38			
250 ppm 41 3.9± 6.2** 500 ppm 37 3.4± 3.6** Ificant difference; *: P ≤ 0.05 **: P ≤ 0.01 Test of Dunnett	125 ppm	34			
500 ppm 37 3.4± 3.6** Ificant difference; *:P ≤ 0.05 **:P ≤ 0.01 Test of Dunnett	250 ppm	41		*	
lficant difference; *:P≤0.05 **:P≤0.01 Test of Dunnett	200 ppm	37		*	
	Significant d:	lifference ;	* : P ≤ 0.05		
	(HCL070)	The state of the s			BAIS 4

WBC (%) BASO MONO LYMPRO OTHER A7± 13 2± 1 0± 0 5± 2 40± 11 6± 18 46± 10 2± 1 0± 0 6± 1 45± 10 1± 1 46± 9 2± 1 0± 0 6± 2 43± 10 1± 1 47± 10 1± 0± 0 6± 2 44± 9 1± 3± 13	MEASURE. TIME : 1 SEX : MALE REPORT TYPE : A1	ALL ANIMALS (105W)						PAGE: 3
13 2± 1 0± 0 5± 2 40± 11 10 2± 1 0± 0 6± 1 45± 10 9 2± 1 0± 0 6± 2 43± 10 10 1± 1 0± 0 6± 2 44± 9	Differential N-BAND		EOSINO	BASO	MONO	LYMPHO		OTHER
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	0 + 1		2± 1	+10			11	+1 9
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	0 = 1		2± 1	+1		1 45±	10	+
$10 1 \pm 1 0 \pm 0 6 \pm 2 44 \pm 9$	0+1		2± 1	+ 0			10	3+
	5.44* 0± 1		1+ 1	+1 0			6	#1

(HCL070)

TABLE F2

HEMATOLOGY: FEMALE

SEA - FEMELE K	MELONI IIIE : AI	111												PAGE :
Group Name NO. of Animals	100	RED BLOOD CELL 1 OF / ml	HEMOGLOBIN g / dl	BIN	HEMATOCRIT %	RIT	MCV f &		мсн р g	A101	MCHC g / d£		PLATELET 1 0³/µl	1
Control 38		7.73± 1.28	14.5±	2.3	39.0∓	5.7	50.7±	3.1	18.8±	0.7	37.1±	1.4	∓899	226
125 ppm 43		8.02± 1.08	14.9±	2.0	40.3±	4.2	50.6±	8. 8.	18.6±	1.1	36.8±	1.8	∓089	222
250 ppm 41		7.92± 1.21	14.9±	2.3	40.1±	5.0	51.3±	ى ئ	18.9±	1.7	36.8±	2.0	∓099	181
500 ppm 37		8.37± 0.40**	15.8±	0.7**	42.4	1.3**	50.7±	1.4	18.8±	0.3	37.2±	0.8	724±	84**

(HCL070)

EX. 1 FEMALE REPORT TYPE : A1 PAGE : 5 Found Name Animal s %1 RETIOLLOCYTE PAGE : 5 Control 38 3.6± 4.9 RETIOLLOCYTE RETIOLLOCYTE 125 ppm 43 3.8± 5.5 Retion Name R	ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] MEASURE. TIME : 1	344/DuCr1Cr1j	[F344/DuCrj]	ALL ANIMALS (105W)	
9 5 7 ** : P ≤ 0.01	SEX : FEMALE	REPORT T	YPE : A1		PAGE
9 4 7 **: P ≤ 0.01	roup Name	NO. of Animals	RETICULOCYTE %		
5 4 7 **: P ≤ 0.01	Control	38			
7 7 ** : P ≤ 0.01	125 ppm	43			
7 ** : P ≤ 0.01	250 ppm	41			
* ★ : P ≤ 0.01	500 ppm	37			
	Significant di	ifference ;	* : P ≤ 0.05	** : P ≤ 0.01	Test of Dunnett

		2	14	22	1	
T) A C	OTHER	5+	4 †I	1+2	1+	
		14	14	14	∞	A Committee of the Comm
	LYMPHO	47±	51±	+ 19	52十	
		2	2	2	*	
	MONO	2 ± 5	2+	2+	+ 9	
		0	0	0	0	A THE
	BASO	+1 0	+1	+1	#1	
	And the second s	1		23	1	Test of Dunnett
	EOSINO	5+	2+	2+	1 1	Test
HEMATOLOGY (SUMMARY) ALL ANIMALS (105W)		14	14	11 *	&	
HEMATOLOGY (SUMMAR) ALE ANIMALS (105W)	WBC (%)	44 +	38+	34±	39∓	
	Differential	1		-		. 01
	Diff N-BAND	1+	1+	1+	∓0.	** : P ≤ 0.01
rj.]	e e	3.73	5. 32	18.80	1.66	0.05
uCrlCrlj[F344/DuC REPORT TYPE : Al	WBC 1 0³ / μβ	5.17±	4. 55±	7.90±	4.40±	VI d *
44/Ducrlcrl REPORT	NO. of Animals	38	43	41	37	ference;
STUDY NO. : 0560 ANUMAL : RAT F344/DuCrlCrlj[F344/DuCrj] MEASURE. TIME : 1 SEX : FEMALE REPORT TYPE : A1	Group Name N	Control	125 ppm	250 ppm	500 ppm	Significant difference ; * : P ≤ 0.05

(HCL070)

TABLE G1

BIOCHEMISTRY: MALE

PAGE: 1	GLUCOSE T-CHOLESTEROL TRIGLYCERIDE mg/dl mg/dl	156± 24 207± 80 184± 131	158± 19 249± 70* 213± 99	155± 23 259± 65** 245± 130	155± 14 260± 79** 274± 126**	
ARY)	T-BILIRUBIN GL	0.17± 0.06	0.16± 0.04	0.20 ± 0.24	0.1** 0.18± 0.08 15	
BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)	N A/G RATIO	0.3 0.8± 0.1	0.2 0.8± 0.1	0.2 0.8± 0.1	0.3** 0.7± 0.1	
/DuCrj] A1	TOTAL PROTEIN ALBUMIN g/dl g/dl	6.7± 0.3 3.0±	6.9± 0.3 3.0±	6.8± 0.2 3.0±	6.7± 0.4 2.8±	
STUDY NO. : 0560 ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj] MEASURE. TIME : 1 SEX : MALE REPORT TYPE : A1	Group Name NO. of TO Animals g	Control 38 6.	125 ppm 34 6.	250 ppm 41 6.	500 ppm 37 6.	

STUDY NO. : 0560 ANTMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] MEASURE. TIME : 1	344/DuCr1Cr1	lj[F344/DuCrj	<u></u>		7	BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)	(SUMMARY) (05W)									
SEX : MALE	REPORT	REPORT TYPE : A1													PAGE:	:
Group Name	NO. of Animals	PHOSPHOLIPID mg/dl)LIPID	AST I U / L	2	ALT I U / g	6	LDH I U / g	e	ALP I U / g	g	G-GTP I U / g	***************************************	CK IU/2	g	
Control	38	302±	114	∓86	116	39+	19	788∓	241	757年	148	7±	4	139±	176	
125 ррш	34	351±	96	∓ 69	18	31+	9	173±	56	166±	*89	+16	വ	+66	26	
250 ppm	41	358±	* 88	+ 98	68	35±	18	187±	127	200∓	69	13±	**	+ 36	21	
	37	364±	111*	¥28	42	41+	24	162±	50	237±	101	17 ±	10**	+ 96	25	
Significant difference ; *: P ≤ 0.05	ifference ;	%	. 05	** : P \leq 0.01	11			Test of Dunnett	nett					ALLAMATA		

	es 	PHORUS						
	PAGE:	INORGANIC PHOSPHORUS		1.4	0.7	0.6	0.6	
		INORGAN mg/d2	T AND THE REST OF	4.4	4.0±	4.1+	4.4±	
				0.6	0.4	0.4	0.8	
		CALCIUM mg/dl		10.8±	10.8±	10.7±	10.9±	
				63	**	2 **	** **	
		CHLORIDE m Eq / 2		105土	107±	110±	112±	
		W		0.4	0.3	0.3	0.3*	119
		POTASSIUM m Eq / &	The state of the s	3.6±	3.7±	3.7±	3.8±	Test of Dunnett
JMMARY) 5W)				23	**	5 **	**	Te
BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)		SODIUM m Eq∕2	THE STATE OF THE S	143±	142±	142 ±	142±	
BION		INE	T THE OPPORTUNITION	0.4	0.1	0.1	0.1	
		CREATININE mg/d2		0.7±	0.6±	0.6±	0.6±	* : P ≤ 0.01
		TROGEN		11.5	4.6	4.9	6.2**	
[F344/DuCrj	KEPUKI IYPE : AI	UREA NITROGEN mg/dl		21.3±	20.6±	20.8±	23.0±	* : P ≤ 0
: 0560 : RAT F344/DuCrlCrlj[F344/DuCrj] TIME : 1	KEPUKI I	NO. of Animals		38	34	41	37	fference ;
STUDY NO. : 0560 ANTWAL : RAT F3. MEASURE. TIME : 1	oea · Male	Group Name		Control	125 ppm	250 ppm	500 ppm	Significant difference; *:P ≤ 0.05

TABLE G2

BIOCHEMISTRY: FEMALE

NO. of TOTAL PROTEIN Animals g/de 38 7.0± 0.4							
10							PAGE: 4
7.0±	ALBUMIN g / dl	A/G RATIO	T-BILIRUBIN mg/dl	GLUCOSE mg/dl	T-CHOLESTEROL mg/d2	TRIGLYCERIDE mg/dl	IDE
		178 pt 100;	The second secon	The state of the s		AT A STATE OF THE	- The second second
	3.6± 0.3	1.1± 0.2	0.14 ± 0.07	143± 18	140± 26	¥78	59
43 7.1± 0.3	3.7± 0.3	1.1± 0.1	0.13 ± 0.04	145± 17	149 ± 35	∓86	64
7.1± 0.3	3.7 ± 0.3	1.1± 0.1	0.15 ± 0.14	148± 19	160± 47	128±	91*
37 6.9± 0.3	3.4± 0.2**	1.0 ± 0.1**	0.12 ± 0.01	149± 13	192± 70**	134±	*68
Significant difference ; * : P ≤ 0.05 ***	* : P ≤ 0.01		Test of Dunnett				

STUDY NO. : 0560 ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj] Miscript True : 1	344/DuCrlCrlj	[F344/DuCrj			B1 AL	BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)	SUMMARY) 35W)								
SEX : FEMALE	REPORT T	REPORT TYPE : A1													PAGE : 5
Group Name	NO. of Animals	PHOSPHOLIPID	LIPID	AST I U / g	í	ALT I U / g	0.000	LDH I U / 2	6	ALP I U / 2	3	6-GTP I U ⁄ g		CK IU/2	
Control	38	256±	48	121±	78	48±	20	212±	81	132±	58	#I %	83	91±	25
125 ppm	43	271±	64	116±	84	48±	21	706±	72	119±	59	#I #3	23	#58	25
250 ppm	41	786±	73	141±	146	+9 9	46	211±	112	131±	75	44	ડ	91#	70
500 ppm	37	324±	110**	∓06	38	43±	18	164±	47*	113±	42	3+	*	75±	22**
Significant d	Significant difference ; * : P ≤ 0.05	*:PS0.		**: P ≤ 0.01	1			Test of Dunnett	nett						

STUDY NO. : 0560 ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj] MRASIDE TIME : 1	344/DuCrlCrl	lj[F344/DuCrj	Ĺį		BIOC	BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)	JUMMARY) 5W)								
SEX : FEMALE		REPORT TYPE : A1													PAGE: 6
Group Name	NO. of Animals	UREA NI	UREA NITROGEN mg/dl	CREATININE ING / d2	INE	SODIUM m Eq / 2		POTASSIUM m.Eq./ &	IUM	CHLORIDE m Eq / 2	m	CALCIUM mg/d2		INORGAN mg / d2	INORGANIC PHOSPHORUS
Control	38	17.1±	1.8	0.5±	0.0	142土	-	3.4	0.4	104±	23	10.5±	0.3	3.7±	0.7
125 ppm	43	17.2±	2.1	0.5±	0.1	142±	-	3.3+	0.4	107±	2**	10.6±	0.4	3.5±	0.7
250 გნთ	41	17.5±	2.0	0.5±	0.0	142±		3.4+	0.4	∓601	5**	10.6±	0.3	3.8	6.0
500 ppm	37	18.0±	2.4	0.5	0.0	140±	* *	3.4	0.3	111	4* *	10.5土	0.4	3.9+	0.6
Significant difference ;	ifference;	* : P ≤ 0.05). 05	** : P ≤ 0.01				Test of Dunnett	mett			PATRICIA DE LA CALLACATA DE LA	AND REAL PROPERTY OF THE PROPE		

TABLE H1

URINALYSIS : MALE

SEX : MALE	REPORT TYPE : A1	YPE : AI									PAGE:
Group Name	NO. of Animals	рН 5.0 6.	0 6.5	7.0	7.5 8	5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI	Protein — + + 2+ 3+ 4+ CHI	Glucose	Ketone body - ± + 2+ 3+ 4+ CHI	Bilirubin - + 2+ 3+ CHI	CHI
Control	42	0 0	9	7	19	8	0 0 0 3 31 8	42 0 0 0 0 0	41 1 0 0 0 0	42 0 0 0	
125 ppm	35	0 0	4	10	14	0 2	0 0 0 2 27 6	35 0 0 0 0 0	35 0 0 0 0 0	35 0 0 0	
250 ppm	42	0 1	9	12	18	0 9	0 0 0 1 25 16	42 0 0 0 0 0	40 1 1 0 0 0	42 0 0 0	
500 ppm	40	0 1	8	13	14	3 1	0 0 0 0 11 29 ***	40 0 0 0 0 0	39 1 0 0 0 0	40 0 0 0	
Significant difference ;	ifference ;	1	* : P ≤ 0.05		d *	** : P ≤ 0.01	Test	Test of CHI SQUARE	000000000000000000000000000000000000000		TO THE PARTY OF TH

SEX : MALE	MET ONL THE - AL				PAGE: 2
Group Name NO. An:	NO. of Animals	Occult blood - ± + 2+ 3+ CHI	Urobilinogen ± + 2+ 3+ 4+ CHI		- And Andrews
			Landania Caranta de Ca		- Average Aver
Control	42	42 0 0 0 0	42 0 0 0 0		
125 ppm	35	35 0 0 0 0	35 0 0 0 0		
250 ppm	42	40 0 1 0 1	42 0 0 0 0		
500 ppm	40	39 0 0 0 1	40 0 0 0 0		
Significant difference ;	erence ;	*: P ≤ 0.05 **	** : P ≤ 0.01	Test of CHI SQUARE	

TABLE H2

URINALYSIS : FEMALE

								4		STREET, STREET	111111111111111111111111111111111111111	0000000	
Group Name	NO. of Animals	5.0	pH 5.0 6.0 6.5 7.0 7.5 8.0 8.5	6.5	7.0	7.5	8.0		CHI	Protein	Glucose	Ketone body - ± + 2+ 3+ 4+ CHI	Bilirubin - + 2+ 3+ CHI
													TOTAL PARTY OF THE
Control	38	0	0	-	က	6	21	4		0 2 7 6 16 7	38 0 0 0 0 0	27 11 0 0 0 0	38 0 0 0
125 ppm	44	0	2	c ₂	7	13	15	2		0 4 6 10 18 6	44 0 0 0 0 0	29 15 0 0 0 0	44 0 0 0
250 ppm	41	0	0	9	11	12	6	က	¥	0 2 5 6 21 7	41 0 0 0 0 0	30 11 0 0 0 0	41 0 0 0
500 ppm	37	0	0	5	7	=======================================	13	_		0 0 0 0 18 19 **	37 0 0 0 0 0	21 16 0 0 0 0	37 0 0 0

(HCL101)

SEX : FEMALE	REPORT TYPE : A1	YPE : A1		PAGE :
Group Name	NO. of Animals	Occult blood - ± + 2+ 3+ CHI	Urobilinogen ± + 2+ 3+ 4+ CHI ·	
Control	38	38 0 0 0 0	38 0 0 0 0	
125 ppm	44	41 2 0 1 0	44 0 0 0 0	
250 ррт	41	40 0 0 0 1	41 0 0 0 0	
200 ppm	37	36 0 0 1 0	37 0 0 0 0	
Significant difference ;	ifference ;	*: P ≤ 0.05 **	** : P ≤ 0.01	Test of CHI SQUARE

TABLE J1

ORGAN WEIGHT, ABSOLUTE: MALE

PAGE:					
	KIDNEYS	2.761± 0.447	2.880± 0.337	2.843± 0.236	2.752± 0.264
	LUNGS	1.390± 0.227	1.405 ± 0.359	1.381± 0.141	1.321± 0.095
	HEART	1.217 ± 0.125	1.207 ± 0.092	1.191 ± 0.088	1.165± 0.141*
SURVIVAL ANIMALS (105W)	TESTES	3.177± 1.347	3.681± 1.275	3.297± 1.276	4.008± 1.605*
SURVIVAI	ADRENALS	0.071± 0.013	0.106± 0.174	0.098± 0.151	0.067± 0.018
344/DuCr.j.]	Body Weight	394± 34	390± 29	380± 26	326± 28**
ANIMAL : KAT F344/DuCrICrIj[F344/DuCrj] REPORT TYPE : A1 SEX : MALE UNIT: g	NO. of Animals	ol 39	.pm 35	pm 41	pm 37
ANIMAL : R REPORT TYPE : SEX : MALE UNIT: g	Group Name	Control	125 ppm	250 թթա	500 ppm

Test of Dunnett

** : P ≤ 0.01

Significant difference ; * : P \leq 0.05

(HCL040)

STUDY NO. 1	ARY)						
LIVER 1. 360 11. 551± 1. 29 0. 400* 12. 328± 1. 68 1. 647* 12. 787± 1. 80 0. 178** 12. 564± 2. 18	WEIGHT:ABSOLUTE (SUMMA AL ANIMALS (105W)	BRAIN	2.032士 0.044				
 	ORGAN Y SURVIV	LIVER					
of mals 9 7	[F344/bucr.j]	SPLEEN	1.337± 1.360		1.240± 1.647*		A STATE OF THE STA
SIUDY NO. : 0560 ANIMAL : RAT F344/1 REPORT TYPE : A1 SEX : MALE UNIT: g Group Name NO. Anii 125 ppm 3% 250 ppm 41	60 IT F344/DuCr1Cr1j[A1	NO. of Animals	1 39	m 35	m 41	m 37	

(HCL040)

TABLE J2

ORGAN WEIGHT, ABSOLUTE: FEMALE

PAGE:: 3						
	YS	0. 131	0.127	0. 128	0.104	
	KIDNEYS	1.720±	1.713±	1.709±	1.758±	
	S	0.065	0.157	0.248	0.049	
	TUNGS	0.928±	0.938±	0.990±	0.947 ±	
		0.061	0.073	0. 086	0.060	
	HEART	0.859±	0.857±	0.882±	0.875±	
E (SUMMARY) 5W)	ES	0.725	0.027	0.126	0.020	
ORGAN WEIGHT:ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (105W)	OVARIES	0. 240±	0.115土	0.139±	0.118±	
ORGAN WE SURVIVAL	ALS	0. 135	0.008	0.013	0.005	
	ADRENALS	0.090 ±	0.068±	0.068±	0.065±	
	(eight	22	24	27	22**	
344/DuCrj]	Body Weight	264±	∓09Z	755±	237±	
344/Ducrlcrlj[F	NO. of Animals	. 38	43	41	37	
STUDY NO. : 0560 ANIMAL : RAT F344/DuCr1J;[F344/DuCrj] REPORT TYPE : A1 SEX : FEMALE UNIT: g	Group Name	Control	125 ppm	250 ppm	200 ppm	

Test of Dunnett

★: P ≤ 0.01

Significant difference ; * : P \leq 0.05

(HCL040)

SEX : FEMALE UNIT: g								PAGE :
Group Name	NO. of Animals	SPLEEN	EEN	LIVER	9R	BRAIN		
Control	38	0.624± 0.289	0.289	€. 690±	1. 131	1.862± 0.040	0.040	
125 ppm	43	0.617±	0.401	€. 759±	1.061	1.836±	0.036**	
250 ppm	41	0.974±	1.775	6.904±	1.462	1. 829 ±	0. 044**	
500 ppm	37	0.526±	0.088	7.039±	0. 689*	1.787 ±	0.029**	
Significant difference ;	lifference;	* : P ≤ 0.05		# : P ≤ 0.01			Test of Dunett	

TABLE K1

ORGAN WEIGHT, RELATIVE : MALE

PAGE: 1						
	KIDNEYS	The state of the s	0.709 ± 0.159	0.740± 0.088 *	0.749± 0.061**	0.848± 0.093**
	LUNGS	Accession of the state of the s	0.357 ± 0.081	0.361± 0.091	0.364± 0.042**	0.408± 0.038**
K)	HEART	TORRONO CONTRACTOR CON	0.311 ± 0.042	0.310± 0.027	0.314± 0.027	0.360± 0.051**
ORGAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS (105W)	TESTES		0.805± 0.334	0.941 ± 0.309	0.868± 0.327	1.237± 0.496**
ORGAN Y SURVIV,	ADRENALS		0.018± 0.004	0.027± 0.047	0.026± 0.043	0.021± 0.005**
[F344/DuCr.j]	Body Weight (g)		394± 34	390 ± 29	380± 26	326± 28**
F344/DuCr1Cr1j	NO. of Animals		39	35	41	37
STUDY NO. : 0560 ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj] REPORT TYPE : Al SEX : WALE UNIT: %	Group Name		Control	125 ppm	250 ppm	500 ppm

Significant difference ; * : P \leq 0.05 (HCL042)

Test of Dunnett

★ : P ≤ 0.01

BAIS 4

Group Name NO. of Animals Animals Control 39 0.349± 0.410 2.954± 0.467 0.519± 125 ppm 35 0.254+ 0.095* 3.161+ 0.371 0.597+	
39 0.349± 0.410 2.954± 0.467 35 0.254+ 0.095* 3.161+ 0.371	BRAIN
35 0 254+ 0 095* 3 161+ 0 371	$0.519\pm\ 0.044$
	$0.527 \pm\ 0.041$
250 ppm 41 0.330± 0.456 3.368± 0.459** 0.535±	$0.535\pm\ 0.035$
500 ppm 37 0.283 \pm 0.064 3.850 \pm 0.517** 0.611 \pm	$0.611\pm\ 0.048**$
Significant difference ; *: P \leq 0.05 **: P \leq 0.01	Test of Dunett

TABLE K2

ORGAN WEIGHT, RELATIVE : FEMALE

	PAGE :							
	4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	KIDNEYS	0.653 ± 0.053	0 661+ 0 046	0.001 - 0.040	0.675 ± 0.064	0.749± 0.091**	
		TUNGS	0.353 ± 0.035	090 0 +898 0	600.0	0.392± 0.113**	0.403± 0.039**	
£		HEART	0.326± 0.028	0 330+ 0 030		0.349± 0.052*	0.373 ± 0.044**	
ORGAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS (105W)	, and the second	OVARIES	0.094 ± 0.293	0.045+ 0.012		$0.056\pm\ 0.054$	0.050± 0.009	
ORGAN SURVIV		ADRENALS	$0.034\pm\ 0.049$	0.026± 0.003		0.027 ± 0.006	$0.028\pm\ 0.004$	**************************************
		body Weight (g)	22	24		27	22**	
[F344/DuCrj]	***************************************	Body	264±	∓092		722年	$237\pm$	
344/DuCrlCrlj	OII.	NU. OI Animals	38	43		41	37	
STUDY NO. : 0560 ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj] REPORT TYPE : A1 SEX : FEWALE	% :.IINn	Group Name	Control	125 ppm		250 ppm	500 ppm	

Test of Dunnett

★ : P ≤ 0.01

Significant difference ; * : P \leq 0.05

(HCL042)

SEX : FEMALE UNIT: %		KEPOKI IYPE : AI SEX : FEMALE UNIT: %			PAGE: 4
Group Name	NO. of Animals	SPLEEN	LIVER	BRAIN	
Control	38	$0.238\pm\ 0.116$	2.532 ± 0.366	0.709± 0.056	
125 ррт	43	0.240 ± 0.163	2.599 ± 0.375	$0.711\pm\ 0.064$	
250 ppm	41	$0.392\pm\ 0.724$	2.719± 0.586*	$0.724\pm\ 0.073$	
500 ppm	37	0.224± 0.041	2.995± 0.378**	0.762± 0.078**	
Significant difference ;	ifference ;	*: P ≤ 0.05 *#:	** : P ≤ 0.01	Test of Dunnett	

TABLE L1

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS : MALE

ALL ANIMALS

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)

STUDY NO. : 056 ANIMAL : RAT REPORT TYPE : A1 SEX : MAL.	: 0560 : RAT F344/DuCr1Cr1j[F344/DuCrj] : A1 : MALE	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)	ON-NEOPLASTIC LESIONS (SUMMARY	£ (A	PAGE: 1
Organ	Group No. of Grade	Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%)	125 ppm 50 . (%) (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%)	500 ppm 50 1 2 3 4 (%) (%) (%)
(Integumentar	[Integumentary system/appandage]				
skin/app	scab	(50) 0 1 0 0 (0) (2) (0) (0)	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	(0)(0)(0)(0) 0 0 0 0 (20)
subcutis	inflammation	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	<pre></pre>	<pre></pre>	<50> 1 0 0 0 (2) (0) (0) (0)
	epidermal cyst		2 0 0 0 (4) (4) (6) (6) (6)	1 0 0 0 (2) (3) (4) (5)	
{Respiratory system}	system)				
nasal cavit	hyperplasia:gland	(0) (0) (0) 0 0 0 0 0 0 (0)	<pre><e0> (0) (0) (0) (0)</e0></pre>	<pre><20> <pre>(0) (0) (0) (0)</pre></pre>	<50> 1 0 0 0 (2) (0) (0) (0)
	eosinophilic change:olfactory epithelium	34 14 0 0 (68) (28) (0) (0)	33 10 0 0 (66) (20) (0) (0)	16 25 4 0 ** (32) (50) (8) (0)	10 34 6 0 ** (20) (68) (12) (0)
	eosinophilic change:respiratory epithelium	26 0 0 0 0 (52) (52) (53) (54) (55)	28 0 0 0 0 (56) (56) (6) (6)	31 0 0 0 (62) (62) (63) (63) (63) (63) (63) (63) (64)	44 0 0 0 ** (88) (0) (0) (0)
Grade 1: Slight <a> a : Number o b b : Number o (c) c : b / a * Significant difference:	1 : Slight 2 : Moderate 3 : Marked a : Number of animals examined at the site b : Number of animals with lesion c : b / a * 100 ifference ; * : P \leq 0.05 ** : P \leq 0.01	rked 4: Severe 1 Test of Chi Square			

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS $(0{\text{--}}105\%)$

STUDY NO. : ANIMAL : REPORT TYPE : SEX :	: 0560 : RAT F344/DuCrlCrlj[F344/DuCrj] : Al : MALE	ALL	HISTOPATHOLOCICAL FINDINGS ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)		PAGE: 2	63
Organ	Findings	Group Name No. of Animals on Study Grade	Control 1 2 3 4 (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%)	500 ppm 50 1 2 3 4 (%) (%) (%) (%)	1
(Respiratory system)	system)						1
nasal cavit	inflammation:foreign body	J	<50> 8 7 0 0 16) (14) (0) (0)	<50> 13 6 0 0 (26) (12) (0) (0)	<50> 9 8 0 0 (18) (16) (0) (0)	<50> 16 10 0 0 (32) (20) (0) (0)	
	inflammation:respiratory epithelium	_	0 1 0 0 0 0) (2) (0) (0)			(0)(0)(0)(0)(0)	
	inflammation:olfactory epithelium	C			1 0 0 0 (2) (2) (3) (4)	1 0 0 0 (2) (2) (3) (4) (4)	
	respiratory metaplasia:olfactory epithelium	ithelium	4 0 0 0 8) (0) (0) (0)	1 0 0 0 (2) (3) (4) (4)	2 0 0 0 (4) (4) (0) (0) (0)	8 0 0 0 0 (16) (16) (16) (16) (16) (16) (16)	
	respiratory metaplasia:gland	Ü	10 0 0 0 20) (0) (0) (0)	12 0 0 0 (24) (0) (0) (0)	8 1 0 0 (16) (2) (0) (0)	15 0 0 0 (30) (30) (30) (30) (30) (30) (30	
	squamous cell metaplasia:respiratory epithelium	y epithelium (3 0 0 0 0 0 0 0 0	(0)(0)(0)(0)(0)			
	atrophy:olfactory epithelium	C	(0) (0) (0) (0 0 0 0 0	0 0 3 0	1 1 0 0 (2) (2) (3) (4)	2 2 1 0 (4)(4)(2)(0)	
lung	congestion	C	<pre></pre>	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	<pre><ep><ep> (0) (0) (0) (0) (0) (0) (0)</ep></ep></pre>	<00 (0) (0) (0) (0) (0) (0) (0) (
Grade 1: Slight <a>> a : Number b b : Number (c) c : b / a * Significant difference:	1: Slight 2: Moderate 3: Para in Number of animals examined at the site b: Number of animals with lesion c: b/a*100 ifference; *: P≤0.05 **: P≤0.	darked 4:5	severe Square				1

SEX :	: A1 : MALE				PAGE
Organ	Group Name No. of Anii Grade	Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%) (%)	500 ppm 50 1 2 3 4 (%) (%) (%) (%)
{Respiratory system}	system)				
lung	edema	(0) (0) (0) (0) 0 0 0 0 <05>	<50> 0 1 0 0 (0) (2) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	<50> (0) (0) (0) (0) (0)
	inflammation		(0)(2)(0)(0)	0 1 0 0 (0) (0) (0) (0)	
	inflammatory infiltration	$\begin{pmatrix} 0 & 1 & 0 & 0 \\ (& 0) & (& 2) & (& 0) & (& 0) \end{pmatrix}$		1 0 0 0 (2) (3) (4) (5)	
	accumulation of foamy cells		1 0 0 0 (2) (2) (3) (4) (4)	(0)(0)(0)(0)(0)	
	bronchiolar-alveolar cell hyperplasia		4 2 0 0* (8)(4)(0)(0)	4 0 0 0 (8) (8) (9) (9)	2 1 0 0 (4) (2) (0) (0)
	inflammation:foreign body			1 0 0 0 (2) (2) (3) (4)	1 0 0 0 () () () ()
{Hematopoietic system}	ic system}				
bone marrow	hemorrhage	(0) (0) (0) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	<pre></pre>	<50> (50) (0) (0) (0) (0)
Grade < a > b b (c)	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: h / a * 100	4 : Severe			

BAIS4

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105#)

STUDY NO. : ANIMAL : REPORT TYPE : SEX :	: 0560 : RAT F344/DuCrlCrlj[F344/DuCrj] : A1 : MALE	HISTOPATHOLOGICAL FINDINGS :: ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%)		PAGE: 4
Огвап	Findings.	Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%) (%)	125 ppm 50 12 3 4 (%) (%) (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%) (%)	500 ppm 50 3 4 (%) (%) (%) (%)
{Hematopoietic system} bone marrow increa	ic system) increased hematopoiesis	<50> 5 0 0 (10) (0) (0) (0)	<pre></pre>	(50) 7 0 0 0 (14) (0) (0) (0)	<50> 5 0 0 0 (10) (0) (0) (0)
	granulopoiesis:increased	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$			
	xanthogranuloma		(0)(0)(2)(0)		(0) (0) (0) (0)
lymph node	lymphadenitis	$\langle 50 \rangle$ 0 1 0 0 (0) (2) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0 0	(0)(0)(0)(0) 0 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 0 0 0 0
spleen	congestion	<50> 2 3 0 0 (4) (6) (0) (0)	<50> 0 2 0 (0) (4) (0) (0)	(50) 0 1 0 0 (0) (2) (0) (0)	(50> 1 0 0 (2) (0) (0) (0)
	hemorrhage	$\begin{pmatrix} 0 & 1 & 0 & 0 \\ (& 0) & (& 2) & (& 0) & (& 0) \end{pmatrix}$			(0)(0)(0)(0)
	deposit of hemosiderin	4 0 0 0 (8) (8) (9) (9) (9)	3 3 0 0 (9) (9)	3 0 1 0 (6) (6) (7) (7)	4 3 0 0 (8) (8) (9) (9)
Grade 1 : Sligh <a>a> a : Numbe b b : Numbe (c) c : b / a Significant difference (IPPI50)	t 2: Moderate r of animals examined at r of animals with lesion : * 100 ; * 100 ; * : P ≤ 0.05 ***	3: Marked 4: Severe the site : P ≤ 0.01 Test of Chi Square			BAIS4

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%)

STUDY NO. : 0560
ANIMAL : RAT F344/Ducricrij[F344/Ducrj]
REPORT TYPE : A1
SEX : MALE

	Group Name No. of Anii	ontrol	125 p pm 50	250 ppm 50	50
Organ	Findings Grade	(%) (%) (%) (%)	(%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	(%) (%) (%) (%)
ematopoiet	(Hematopoietic system)				
spleen	fibrosis:focal	<50> 1 0 0 (2) (0) (0) (0)	<pre></pre>	<pre></pre>	<50> 0 0 0 0 (0) (0) (0)
	increased extramedullary hematopoiesis	7 3 0 0 (14) (6) (0) (0)	4 2 2 0 (8)(4)(4)(0)	1 4 0 0 (2) (8) (0) (0)	2 3 1 0 (4) (6) (2) (0)
(Circulatory system)	r system)				
heart	myocardial fibrosis	<50> 29 1 0 0 (58) (2) (0) (0)	<50> 23 1 0 0 (46) (2) (0) (0)	$\langle 50 \rangle$ 20 1 0 0 (40) (2) (0) (0)	<50> 20 2 0 (40) (4) (0) (0)
(Digestive system)	ystem)				
oral cavity	squamous cell hyperplasia	(0) (0) (0) (0) 0 0 0 0 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 <00>	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	<50> 1 0 0 0 (2) (0) (0) (0)
esophagus	inflammation	<50> 0 1 0 0 (0) (2) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 (0) (0) (0
Grade < a > b	1 : Slight 2 : Moderate 3 : Marked a : Number of animals examined at the site b : Number of animals with lesion	4 : Severe			

BAIS4

STUDY NO. ANIMAL REPORT TYPE SEX	: 0560 : RAT F344/DuCrlCrlj[F344/DuCrj] : A1 : MALE		HISTOPATHOLOGICAL FINDINGS :N ALL ANIMALS (0-105W)	STOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) L ANIMALS (0-105W)		PAGE: 6
Organ	Findings	Group Name No. of Animals on Study Grade	control 50 4 (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%)	500 ppm 50 1 2 3 4 (%) (%) (%)
(Digestive system)	system)					
stomach	ulcer:forestomach		<pre></pre>	<50> 2 1 0 0 (4) (2) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	(50> 1 1 4 1 (2) (2) (8) (2)
	hyperplasia:forostomach		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	3 1 0 0 (6) (2) (0) (0)	0 0 1 0 (0) (0) (0) (0)	3 2 0 0 (6) (7) (9) (9)
	erosion:glandular stomach		3 0 0 0 (0) (0) (0)	4 0 0 0 (8) (8) (9) (9)	2 1 0 0 (4) (5) (7) (7)	7 0 0 0 0 (14) (14) (0) (0) (0)
	ulcer:glandular stomach		0 3 0 0 0 0 0 0 0	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	2 0 0 0 (4) (4) (6) (6) (6)	3 1 0 0 (6) (2) (0) (0)
	hyperplasia:glandular stomach		3 0 0 0 0 (0) (0) (0)	5 0 0 0 0 (10) (10) (10) (10)	2 0 0 0 (4) (4) (6) (6)	4 0 0 0 (8) (8) (9) (9)
	mineralization:glandular stomach		(0)(2)(2)(0)	(0)(0)(0)(0)(0)		
	dilated glands		1 0 0 0 (2) (3) (4) (4)			
small intes	erosion		(0)(0)(0)(0) 0 0 0 0 0 0 0 0	<50> 4 0 0 0 (8) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 0 0 0 0
Grade <a>> b	1: Slight 2: Moderate 3: Na a: Number of animals examined at the site b: Number of animals with lesion	3 : Marked the site	4: Severe			

BAIS4

Test of Chi Square

** : $P \le 0.01$

(c) c:b/a*100 Significant difference; *: P \leq 0.05

(SUMMARY)	
:NON-NEOPLASTIC LESIONS (
HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)	ALL ANIMALS (0-105W)

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE

Digestive system	OrganFindings	No. of Animals on Study Grade	s on Study 50 (%) (%) (%) (%)	125 ppm 50 (%) (%) (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%)	500 ppm 50 1 2 3 4 (%) (%) (%) (%)
Herriation Cast C	gestive system)					
al (0) (0) (0) (0) (0) (0) (0) (0			<50> 0 0 0) (0) ((50) (0) (0) (0)	(20) (0) (0) (0) (0)	<pre></pre>
entral (0) (0) (0) (0) (0) (0) (0) (0	hemorrhage		0 0 0 0	1 0 0 2 2) (0) (0) (0 0 0 0	0 0 0 0
entral (0) (0) (0) (0) (0) (0) (0) (0	necrosis:central		0 0 0 0	1 2 0 2) (4) (0) (0 0 0 0	0 2 0 0) (4) (0)
$ \begin{pmatrix} 0 & 2 & 1 & 0 & 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0$	necrosis:focal		0 0 0 0	0 0 0 0	1 0 0 2 2) (0) (0) (1 0 0 2) (0)
$ \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0$	fatty change		0 2 1 0) (4) (2) (1 1 1 2) (2) (2) (0 0 0 0	0 0 0 0
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	fatty change:centr	al	0 0 0 0	0 0 0 0	0 0 0 0	1 0 0 2) (0) (0)
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	fatty change:perip	oheral	0 1 0 0) (2) (0) (0 0 0 0	0 0 0 0	0 0 0 0
	degeneration:centr	al	0 0 0 0	1 0 0 2) (0) (0 0 0 0	0 0 0 0

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%)

STUDY NO. ANIMAL REPORT TYPE SEX	: 0560 : RAT F344/DuCrlCrlj[F344/DuCrj] : A1 : MALE		HISTOPATHOLOGICAL FINDI ALL ANIMALS (0-105W)	INGS :NON-	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)		PAGE: 8
Organ	Findings.	Group Name No. of Animals on Str Grade	Control 1 2 3 (%) (%) (%)	(%)	125 ppm 50 1 2 3 4 (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%) (%)	500 ppm 50 1 2 3 4 (%) (%) (%)
{Digestive system}	ystem}						
liver	granulation		<50> 3 0 0 (6) (0) (0) (0 (0	(0) (0) (0) (0) 0 0 0 0 0 0 0 0 0	<50> 2 0 0 (4) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 <05>
	clear cell focus		$\begin{pmatrix} 7 & 1 & 0 \\ (14) & (2) & (0) \end{pmatrix}$	0 (0	11 3 0 0 (22) (6) (0) (0)	8 0 0 0 (16) (16) (16) (16)	6 0 0 0 (12) (12) (13) (13) (13) (14) (15)
	acidophilic cell focus		(2) (2) (0) (0 (0	3 0 0 0 0 (9) (9)	1 0 0 0 (2) (2) (3) (4)	1 0 0 0 (2) (3) (4) (4)
	basophilic cell focus		5 0 0 (10) (10) (10) (10) (10) (10)	0 (0	3 1 0 0 (6) (7) (7) (7)	5 3 0 0 (10) (10) (10) (10)	5 2 0 0 (10) (4) (0) (0)
	spongiosis hepatis		3 1 0 (6) (2) (0) (0 (0	4 0 0 0 0 (8) (8) (9) (9)	4 0 0 0 (8) (8) (8) (8) (8) (8)	1 0 0 0 (2) (2) (3) (4)
	bile duct hyperplasia		7 42 0 (14) (84) (0) (0 0	9 40 0 0 (18) (80) (0) (0)	2 47 0 0 (4) (94) (0) (0)	5 45 0 0 (10) (90) (0) (0)
pancreas	atrophy		<50> 9 8 1 (18) (16) (2) (0 0	<50> 5 4 0 0 (10) (8) (0) (0)	<50> 9 2 2 0 (18) (4) (4) (0)	<50> 5 5 0 0 (10) (10) (0) (0)
	islet cell hyperplasia		1 2 0 (2) (4) (0) (0 (0	2 1 2 0 (4) (2) (4) (0)	1 1 0 0 (2) (2) (3) (4)	(2) (0) (0) (0)
Grade 1 : Slight <a> a : Number b b : Number (c) c : b / a * Significant difference;	2 : Moderate of animals examined of animals with lesi 100 *:P≤0.05	3 : Marked site ≤ 0.01	4 : Severe Test of Chi Square				

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)

STUDY NO. : ANIMAL : REPORT TYPE : SEX :	: 0560 : RAT F344/DuCrlCrlj[F344/DuCrj] : A1 : MALE		HISTOPATHOLOCICAL FINDINGS :N ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)		PAGE	თ ო
Organ	Findings	Group Name No. of Animals on Study Grade	Control S on Study 50 1 2 3 4 (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%) (%)	500 ppm 50 (%) (%) (%) (%)	<u>4</u> %
(Urinary system) kidney	tem) ectopic tissue		(20) (0) (0) (0) (0) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	(50) (0) (0) (0) (0) (0) (0) (0) (0) (0) (0 6
	cyst			(0)(0)(0)(0)(0)		1 0 0 0 () () ()	0 (0
	scar			1 0 0 0 (2) (3) (4) (5)			0 (0
	chronic nephropathy		11 22 11 5 (22) (23) (10)	16 14 17 0 * (32) (28) (34) (0)	8 18 22 0 * (16) (36) (44) (0)	8 25 16 1 (16) (50) (32) (2	2)
	hydronephrosis			1 0 0 0 (2) (3) (4) (5)			0 (0
	tubular necrosis		$\begin{pmatrix} 0 & 1 & 0 & 0 \\ (& 0) & (& 2) & (& 0) & (& 0) \end{pmatrix}$				0 (0
	papillary necrosis			0 0 1 0 (0) (0) (0) (0)		0) (0) (0) (0)	0 (0
	mineralization:papilla		1 0 0 0 (2) (2) (3) (4)				0 (0
Grade 1 : Slight <a> a : Number b b : Number (c) c : b / a * Significant difference;	2 : Moderate of animals examined of animals with lesi : 100 * : P ≤ 0.05	Marked .01	4 : Severe Test of Chi Square				

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%) STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE

		10.	125 ppm 50	250 ppm 50	500 ppm 50
Organ	Findings.	(%)	(%) (%) (%) (%)	(%) (%) (%) (%)	(%) (%) (%) (%)
(Urinary system)	stem)				
kidney	mineralization:pelvis	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	<50> 3 0 0 (6) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	<50> 2 0 0 0 (4) (0) (0) (0)
	urothelial hyperplasia:pelvis	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	2 0 0 0 (4) (4) (6) (6) (6)	2 1 1 0 (4)(2)(2)(0)	2 2 0 0 (4) (4) (6) (7)
	atypical tubule hyperplasia	$\begin{pmatrix} 0 & 1 & 0 & 0 \\ (& 0) & (& 2) & (& 0) & (& 0) \end{pmatrix}$	(0)(0)(0)(0)	(0)(0)(0)(0)(0)	
urin bladd	dilatation	(0) (0) (0) (0) 0 0 0 0 0 <05>	<00) (0) (0) (0) (0) (0) (0) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)
	inflammation		1 0 0 0 (2) (2) (3) (4)		
(Endocrine system)	system}				
pituitary	cyst	(0) (0) (0) (0) 0 0 0 0 (0) (0)	<pre></pre>	<pre></pre>	(50) 0 1 0 0 (0) (2) (0) (0)
Grade	1: Slight 2: Moderate 3:] a : Number of animals examined at the site b : Number of animals with lesion	3 : Marked 4 : Severe			

BAIS4

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)

STUDY NO. : 0560

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

REPORT TYPE : A1

SEX : MALE

	1000		THE PARTY OF THE P		
Organ	Findings	Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%) (%)	500 ppm 50 1 2 3 4 (%) (%) (%) (%)
{Endocrine system}	(stem)				10000000
pituitary	hyperplasia	(50) 2 9 0 0 (4) (18) (0) (0)	<50> 3 10 0 (6) (20) (0) (0)	<50> 2 6 0 0 (4) (12) (0) (0)	(50) 0 1 0 0 ** (0) (2) (0) (0)
	Rathke pouch		2 1 0 0 (4) (2) (0) (0)	1 0 0 0 (2) (2) (3) (4) (4)	3 0 0 0 0 0 0 0
thyroid	follicular hyperplasia	(0) (0) (0) (0) 0 0 0 0 <05>	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	<50> 1 0 0 0 (2) (0) (0) (0)	(50) 2 0 0 (4) (0) (0) (0)
	C-cell hyperplasia	14 4 1 0 (28) (8) (2) (0)	13 3 2 0 (26) (6) (4) (0)	13 6 0 0 (26) (12) (0) (0)	14 2 0 0 (28) (4) (0) (0)
adrenal	ossecus metaplasia	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 <02>
	hyperplasia:medulla	(2) (10) (0) (0)	1 3 0 0 (2) (2) (6) (0) (0)	1 2 0 0 (2) (4) (0) (0)	0 1 0 0 (0) (0) (0) (0)
	focal fatty change:cortex		0 1 0 0 (0) (0) (0) (0)	1 0 0 0 (2) (3) (4) (4)	
Grade < a > b b (c)	Grade 1 : Slight 2 : Moderate 3 :) <a> a : Number of animals examined at the site b b : Number of animals with lesion (c) c : b / a * 100	3 : Marked 4 : Severe at the site			

BAIS4

Test of Chi Square

**: P ≤ 0.01

* : P ≤ 0.05

Significant difference;

(HPT150)

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STUDY NO. : ANIMAL : REPORT TYPE : SEX :	: 0560 : RAT F344/DuCrlCrlj[F344/DuCrj] : Al : MALE	HISTOPATHOLOGICAL FINDINGS :: ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)	. 0	PAGE : 12
Organ	Findings	Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	250 ppm 50 1 2 3 4 (%) (%) (%)	500 ppm 50 1 2 3 4 (%) (%) (%) (%)
(Reproductive system)	system)				
testis	mineralization	$ \begin{array}{c cccc} $	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	<00 (0) (0) (0) (0) (0) (0) (0)	<pre></pre>
	arteritis	$\begin{pmatrix} 0 & 1 & 0 & 0 \\ (& 0) & (& 2) & (& 0) & (& 0) \end{pmatrix}$		(0)(0)(0)(0)(0)	(0)(0)(0)(0)(0)
	interstitial cell hyperplasia	15 1 0 0 (30) (2) (0) (0)	9 1 0 0 (18) (2) (0) (0)	7 0 0 0 0 (14) (14) (0) (0) (0)	8 0 0 0 0 0 (16)
prostate	inflammation	<50> 2 0 0 0 (4) (0) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
	hyperplasia	12 1 0 0 (24) (2) (0) (0)	7 5 0 0 (14) (10) (0) (0)	6 2 0 0 (12) (4) (0) (0)	6 1 0 0 (12) (2) (0) (0)
(Nervous system) brain	tem) necrosis:focal	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 0 000>	(0)(0)(0)(0) 0 0 0 0 0 0 0 0 0
Grade 1 : Slight <a> a > a : Number b	1 : Slight 2 : Moderate 3 :) a : Number of animals examined at the site b : Number of animals with lesion c : b / a * 100 ifference : * : P \leq 0.05 ** : P \leq 0.	3: Marked 4: Severe e site P ≤ 0.01 Test of Chi Square			

BAIS4

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%)

STUDY NO. : 0560 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] REPORT TYPE : A1 SEX : MALE	HISTOPATHOLOGICAL FINDINGS :N ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)		PAGE: 13
Organ Findings	Group Name Control No. of Animals on Study 50 Grade (%) (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%) (%)	500 ppm 50 1 2 3 4 (%) (%) (%) (%)
{Nervous system} brain mineralization	(0) (0) (0) (0) 0 0 0 0 0 <05>	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 0 0 (0) (0) (0)	(50) 0 1 0 0 (0) (2) (0) (0)
dilatation:cerebral ventricle	(0)(2)(0)(0)			
(Special sense organs/appendage)				
eye cataract	$\langle 50 \rangle$ 3 2 0 0 (6) (4) (0) (0)	<50> 1 1 0 0 (2) (2) (0) (0)	(50) 3 1 0 0 (6) (2) (0) (0)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
retinal atrophy	2 3 2 0 (4) (6) (4) (0)	0 0 1 1 (0) (0) (0) (0) (0) (0)	0 1 1 0 (0) (2) (2) (0)	0 1 2 2 (0) (2) (4) (4)
keratītīs	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		(0)(0)(0)(0)(0)	1 0 0 0 (2) (2) (3) (4) (4)
iritis				0 1 0 0 (0) (0) (0) (0)
degeneration:cornea	3 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		(0)(0)(0)(0)(0)	2 0 1 0 (4) (4) (5) (5) (6)
Grade 1: Slight 2: Moderate ⟨a⟩ a: Number of animals examined at b : Number of animals with lesion (c) c: b/a*100 Significant difference; *: P ≤ 0.05 ***	3 : Marked 4 : Severe the site : P ≤ 0.01 Test of Chi Square			

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%)

STUDY NO. : ANIMAL : REPORT TYPE : SEX :	: 0560 : RAT F344/DuCrlCrlj[F344/DuCrj] : A1 : MALE	HISTOPATHOLOGICAL FI ALL ANIMALS (0-105W)	LOGICAL FINDINGS :N S (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-1059)		PAGE: 14
Organ	Findings	Group Name No. of Animals on Study Grade (%)	Control 50 4 (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%) (%)	500 ppm 50 1 2 3 4 (%) (%) (%) (%)
(Special sens	(Special sense organs/appendage)					
eye	squamous cell metaplasia:cornea	0 0	<50> 0 0 0 0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	<00 (0) (0) (0) (0) (0) (0)	(0)(0)(0)(0) 0 0 0 0 0 0 0 0
Harder gl	lymphocytic infiltration	0	<50> 0 0 0 0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	<50> 1 0 0 0 (2) (0) (0) (0)
nasolacr d	inflammation	0 0	<20> (0) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	<50> 0 2 0 (0) (4) (0) (0)	(50) (2) (0) (0)
{Body cavities}	{\$					
peritoneum	abscess) (0) 0	<20> 0 0 0 0) (0)	<pre></pre>	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	<50> 1 0 0 0 (2) (0) (0) (0)
Grade 1 : Slight <a> a : Number b b : Number (c) c : b/a* Significant difference;	2 : Moderate of animals examined of animals with lesi * 100 * : P ≤ 0.05	3: Marked 4: Severe at the site on Test of Chi Square				

TABLE L4

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS : FEMALE

ALL ANIMALS

00 ୦ ଚ 00 00 00 o 6

Test of Chi Square

≤ 0.01

.. ∀ *

* : $P \le 0.05$

(HPT150)

PAGE: 15 500 ppm 0 3 0 (0) (0) (0 1 21 28 (2) (42) (56) (37 11 0 (74) (22) (0) (2 0 0 (4) (0) (0) (3 0 0 (9) 2 (%) 1 0 0 (2) (2) (3) 4 8 00 (0)(0)(0)(0)(0) 00 o 6 00 00 00 250 ppm 0 1 0 (0) (2) (0) (2 3 (%) (%) 0 28 22 (0) (56) (44) (38 11 0 (76) (22) (0) (0 (0) (0) (0) (0)(2)(0)(o 6 5 0 (10) (10) (10) -188 4 8 00 o 6 o 6 00 00 1 0 0 () () () -- 6 2 3 (%) (%) (1 0 0 (2) (2) (0) (41 7 0 (82) (14) (0) () 00 mdd 0 0 0 0 1 31 17 (2) (62) (34) (125] . 6 1 1 (2) (2) (3 (9 2 3 4 (%) (%) (%) 00 00 00 00 00 00 00 Control) 0 0 0 0 0 0 0 0 0 0 37 7 0 (74) (14) (0) (2 0 0 (4) (4) (0) (1 28 20 (2) (56) (40) (1 0 0 (2) (2) (0) (1 0 (-|8 Group Name No. of Animals on Study 3 : Marked respiratory metaplasia:olfactory epithelium eosinophilic change:respiratory epithelium eosinophilic change:olfactory epithelium a : Number of animals examined at the site b : Number of animals with lesion inflammation:respiratory epithelium 2 : Moderate inflammation:foreign body goblet cell hyperplasia [Integumentary system/appandage] c:b/a*100 Findings (Respiratory system) nasal cavit subcutis Organ

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%)

STUDY NO. : 0560
ANIMAL : RAT F344/Ducrlcrlj[F344/Ducrj]
REPORT TYPE : A1
SEX : FEMALE

STUDY NO. ANIMAL REPORT TYPE SEX	: 0560 : RAT F344/DuCrlCrlj[F344/DuCrj] ?: A1 : FEMALE	HISTOPATHOLOGICAL FINDINGS ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)		PAGE: 16
Organ	Findings	Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%)	500 ppm 50 1 2 3 4 (%) (%) (%) (%)
(Respiratory system)	y system)				
nasal cavit	respiratory metaplasia:gland	<50> 14 0 0 0 (28) (0) (0) (0)	<50> 15 2 0 0 (30) (4) (0) (0)	<50> 16 0 0 0 (32) (0) (0) (0)	<50> 16 1 0 0 (32) (2) (0) (0)
	atrophy:olfactory epithelium		2 0 0 0 (4) (4) (6) (6) (6)		0 0 0 0 0
Jarynx	inflammation	<20> (0) (0) (0) (0) (0)	(0)(0)(0)(0) 0 0 0 0 (0)(0)(0)	(0) (0) (0) (0) 0 0 0 0 (0) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)
lung	edema	<50> (0) (0) (0) (0) (0)	<00 (0) (0) (0) (0) (0) (0) (0) (<50> 1 0 0 0 (2) (0) (0) (0)	<pre><20> <pre>(0) (0) (0) (0)</pre></pre>
	inflammatory infiltration			1 0 0 0 (2) (3) (4) (4)	1 0 0 0 (2) (2) (3) (4)
	accumulation of foamy cells	1 0 0 0 (2) (3) (4) (6) (6)	2 0 0 0 (4) (4) (6) (6) (6)		$\begin{pmatrix} 1 & 1 & 0 & 0 \\ (2) & (2) & (0) & (0) \end{pmatrix}$
	bronchiolar-alveolar cell hyperplasia	sia 1 0 0 0 (2) (3) (6) (6)	2 0 0 0 (4) (4) (6) (6)	3 0 0 0 0 (0) (9)	
Grade < a >	1: Slight 2: Moderate 3::) a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	harked 4:9			
חושטדדרמווני	. r ls 0.05				

BAIS4

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS $(0{\text{--}}105\%)$

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlcrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE

Organ	Ga N Ga Findings	Group Name Control No. of Animals on Study 50 Grade (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%) (%)	500 ppm 50 1 2 3 4 (%) (%) (%) (%)
(Respiratory system)	ystem}				
lung	inflammation:foreign body	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	<00 (0) (0) (0) (0) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)	<00 \ (0) (0) (0) (0) (0)
(Hematopoietic system)	system)				
bone marrow	granulation	(0) (0) (0) (0) 0 0 0 0 <05>	\$ (6) (7) (8) (9) (9) (9)	<pre></pre>	(0) (0) (0) (0) 0 0 0 0 0 (0) (0)
	increased hematopoiesis	6 1 0 0 (12) (2) (0) (0)	4 1 0 0 (8)(2)(0)(0)	4 2 0 0 (8) (4) (0) (0)	6 1 0 0 (12) (2) (0) (0)
spleen	atrophy	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	<50>	(0) (0) (0) (0) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0 0
	congestion			1 0 0 0 (2) (3) (4) (5)	0 1 1 0 (0) (2) (2) (0)
	deposit of hemosiderin	28 6 0 0 (56) (12) (0) (0)	30 7 0 0 (60) (14) (0) (0)	25 12 0 0 (50) (24) (0) (0)	33 9 1 0 (66) (18) (2) (0)
Grade 1	1: Slight 2: Moderate 3:] a: Number of animals examined at the site b: Number of animals with lesion	3 : Marked 4 : Severe			

BAIS4

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS $(0-105 \ensuremath{\mathrm{W}})$

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlclj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE

		THE TAXABLE THE PROPERTY OF TH			PAGE :
Organ	Group Name No. of Animals on Study Grade Findings (%)	Study 50 4 (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%) (%)	500 ppm 50 1 2 3 4 (%) (%) (%) (%)
dematopoie	(Hematopoietic system)				
spleen	fibrosis:focal	<50> (0) (0) (0) (0) (0)	(50) 2 0 0 0 (4) (0) (0) (0)	(6) (6) (6) (6) 0 0 0 0 0 (0) (0)	(20) (0) (0) (0) (0) (0) (0)
	increased extramedullary hematopoiesis	8 3 1 0 (16) (6) (2) (0)	2 4 0 0 (4) (8) (0) (0)	3 4 1 0 (6) (8) (2) (0)	4 4 2 0 (8)(8)(4)(0)
irculator	(Circulatory system)				
heart	necrosis:focal	(0) (0) (0) (0) 0 0 0 0 (0) (0) (0) (0)	(0)(0)(0)(0) 0 0 0 0 0 (0)(0)	<50> (50) (0) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)
	myocardial fibrosis	6 0 0 0 (12) (12) (13) (13) (14)	11 0 0 0 (22) (22) (0) (0) (0)	5 0 0 0 (10) (10) (10) (10)	8 0 0 0 (16) (16) (16) (16) (16)
(Digestive system) esophagus in	system) inflammation	(0) (0) (0) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 . <05>	(50) 1 0 0 0 (2) (0) (0) (0)	(0)(0)(0)(0)

BAIS4

Test of Chi Square

**: P ≤ 0.01

(HPT150)

Grade 1: Slight 2: Moderate 3: Ma < a > a : Number of animals examined at the site b : Number of animals with lesion (c) c: b/a*100 Significant difference; *: P \leq 0.05 **: P \leq 0.0

4 : Severe

3 : Marked

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105#)

STUDY NO. ANIMAL REPORT TYPE SEX	: 0560 : RAT F344/DuCrlCrlj[F344/DuCrj] E : A1 : FEMALE	HISTOPATHOLOGICAL FI ALL ANIMALS (0-105W)	. (0-105#)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)		PAGE: 19
Огдал	Findings	Group Name No. of Animals on Study Grade (%)	Control 50 2 3 4 (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%)	500 ppm 50 1 2 3 4 (%) (%) (%) (%)
{Digestive system}	system)					
stomach	inflammation	0 0	<50> 0 0 0 0) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	(0)(0)(0)(0) 0 0 0 0 0 0 0 0
	ulcer:forestomach	1 (2) (0 0 1 0) (0) (2)	0 2 0 (0) (0) (0) (0)	0 1 1 0 (0) (2) (2) (0)	3 1 0 0 (6) (2) (0) (0)
	hyperplasia:forestomach	2 (4) ((0) (0) (0	1 1 1 0 (2) (2) (0)	0 1 0 0 (0) (0) (0)	3 0 0 0 0 (0) (9)
	erosion:glandular stomach	0 0	(0) (0) (0		1 0 0 0 (2) (2) (3) (4)	1 0 0 0 (2) (2) (3) (4) (5)
	ulcer:glandular stomach	2) (4)	(0) (0) (0		1 2 0 0 (2) (4) (0) (0)	2 0 0 0 (4) (4) (6) (6) (7)
	hyperplasia:glandular stomach	1 (2) ((0) (0) (0			
small intes	erosion	0)	<50> 0 0 0 0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 (0) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)
liver	herniation	15 (30) (<50> 0 0 0 0) (0) (0)	<50> 8 0 0 0 (16) (0) (0) (0)	<50> 9 0 0 0 (18) (0) (0) (0)	<50> 8 0 0 0 (16) (0) (0) (0)
Grade (a) b b (c) Significant	Grade 1: Slight 2: Moderate 3:) <a> a : Number of animals examined at the site b : Number of animals with lesion (c) b / a * 100 Significant difference : *: P \leq 0.05 **: P \leq 0.	3: Marked 4: Severe at the site on Test of Chi Square				

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANTMALS (0-105%)

STUDY NO. SAVIMAL SEX	: 0560 : RAT F344/DuCrlCrlj[F344/DuCrj] : Al : FEMALE		HISTOPATHOLOGICAL ALL ANIMALS (0-103	FINDINGS :N 5W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)		PAGE: 20
Organ	Findings	Group Name No. of Animals on Study Grade	1 2 50 %) (%)	Control 3 4 (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%) (%)	500 ppm 50 1 2 3 4 (%) (%) (%)
{Digestive system}	ystem}						
liver	peliosis-like lesion		<50> 1 0 ((2) (0) (((O) (O O O	<pre></pre>	<50> 1 0 0 0 (2) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0
	necrosis:central		1 0 (2) (3) (6)	0 0		0 2 0 0 (0) (0) (0) (0)	4 0 0 0 (8) (8) (9) (9)
	necrosis:focal		3 2 (0 0	2 0 0 0 (4) (4) (6) (6)	3 0 0 0 0 (0) (9)	2 1 0 0 (4)(2)(0)(0)
	fatty change		0 2 ((O) (O O 0			
	fatty change:central		0 0 0	0 0			0 1 0 0 (0) (0) (0) (0)
÷	lymphocytic infiltration		0 2 0 (0) (4) (0)	0 (0 0	0 1 0 0 (0) (0) (0) (0)		
	granulation		7 3 (0 0	5 1 0 0 (10) (2) (0) (0)	5 0 0 0 (10) (10) (10) (10)	10 0 0 0 (20) (20) (0) (0)
	inflammatory cell nest		1 0 (2) (3) (1)	(0) (0 0 0			
Grade 1 : Slight <a> a : Number b b : Number (c) c : b / a * Significant difference;	1: Slight 2: Moderate 3:) a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 difference; *: P ≤ 0.05 **: P ≤ 0.05	farked 01	4 : Severe Test of Chi Square				

STUDY NO. ANIMAL REPORT TYPE SEX	: 0560 : RAT F344/DuCr1Cr1j[F344/DuCrj] : A1 : FEMALE	HISTOPATHOLOCICAL FINDING ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)	C	PAGE: 21
Organ	Findings	Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%) (%)	125 ppm 50 (%) (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%) (%)	500 ppm 50 1 2 3 4 (%) (%) (%)
(Digestive system)	system)				
liver	fibrosis	(0) (0) (0) (0) 0 0 0 0 <0\$>	<50> 0 1 0 0 0 (2) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 0 <000>
	clear cell focus	$\begin{pmatrix} 1 & 1 & 0 & 0 \\ (2) & (2) & (2) & (0) & (0) \end{pmatrix}$	1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	3 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 1 0 0 (0) (0) (0) (0)
	basophilic cell focus	17 5 0 0 (34) (10) (0) (0)	31 4 0 0 (42) (8) (0) (0)	22 0 0 0 (44) (44) (0) (0) (0)	9 1 0 0* (18) (2) (0) (0)
	bile duct hyperplasia	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	6 1 0 0 (12) (2) (0) (0)	3 1 0 0 (6) (7) (10) (10)	(2) (2) (0) (0)
pancreas	atrophy	<50> 1 0 0 0 (2) (0) (0) (0)	<50> 1 0 0 0 0 (2) (0) (0) (0)	<50> 4 1 0 0 (8) (2) (0) (0)	(6) (0) (0) (0) (0)
	islet cell hyperplasia		0 1 0 0		
(Urinary system))				
kidney	chronic nephropathy	<50> 39 7 0 0 (78) (14) (0) (0)	<50> 39 7 0 0 (78) (14) (0) (0)	<50> 38 6 1 0 (76) (12) (2) (0)	<50> 36 10 3 0 (72) (20) (6) (0)
Grade < a > b (c) Significant	Grade 1: Slight 2: Moderate 3:) <ab></ab> \langle a > a : Number of animals examined at the site b : Number of animals with lesion (c) c:b/a*100 Significant difference; *:P \leq 0.05 **:P \leq 0.	3: Marked 4: Severe at the site on Test of Chi Square			

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HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)	
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SAI	(0-105W)
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STUDY NO. : 056 ANIMAL : RAT REPORT TYPE : A1 SEX : FEM	: 0560 : RAT F344/DuCrlCrlj[F344/DuCrj] : Al : FEMALE	HISTOPATHOLOGICAL FI ALL ANIMALS (0-105W)	SICAL FINDINGS : (0-105#)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)	(,2)	PAGE: 22
Organ	Findings	Group Name No. of Animals on Study Grade (%) (%)	Control 50 3 4 0 (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%) (%)	500 ppm 50 1 2 3 4 (%) (%) (%) (%)
(Urinary system)	ŋ					
kidney	hydronephrosis	(0) (0) 0 0	<50> (50) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 (20)
	tubular necrosis	(0) (0)	(0)(0)(2 0 0 0 (4) (4) (6) (6) (6)	(0) (0) (0) (0) 0 0 0 0
	mineralization:papilla	2 0 (4) (0)	0 0 0			2 0 0 0 (4) (4) (6) (6) (6)
	mineralization:pelvis	(0) (0) 0 0	0 0 0	(0)(0)(0)(0)	3 0 0 0 0 (0) (0) (0)	4 0 0 0 0 (8) (8) (9) (9)
	desquamation:pelvis	(2) (0)	0 0 0	2 0 0 0 (4) (4) (6) (6)	2 1 0 0 (4) (2) (0) (0)	1 0 0 0 (2) (2) (3) (4)
	urothelial hyperplasia:pelvis	(0) (2)	0 0 0	(2) (0) (0) (0)	1 0 0 0 (2) (3) (4) (5)	1 0 0 0 (2) (2) (3) (4)
	atypical tubule hyperplasia	(0) (0)	0 0 0	(0)(0)(0)(0)	1 0 0 0 (2) (3) (4) (5)	(0)(0)(0)(0)
urin bladd	dilatation	(0) (0) 0 0 0 (0) (0)	<50>) 0 0)) (0) (0)	<50> 0 0 0 0 (0) (0) (0)	(6) (0) (0) (0) 0 0 0 0 0 0 0 0 0 0	(50) 1 0 0 0 (2) (0) (0) (0)
Grade 1 : Slight <a>a> a : Number b b : Number (c) c : b/a* Significant difference;	2 : Moderate of animals examined of animals with lesi r 100 * : P \leq 0.05	3 : Marked 4 : Severe at the site on $**$ + : P \leq 0.01 Test of Chi Square				

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)

STUDY NO. : ANTMAL : REPORT TYPE : SEX :	: 0560 : RAT F344/DuCrlCrlj[F344/DuCrj] : Al : FEMALE	HISTOPATHOLOGICAL FINDINGS : ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)	: C	66 - 15VMG
Organ	Findings_	Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%) (%)	. ,
(Urinary system)	rem) transitional cell hyperplasia	<50> 0 1 0 0 (0) (2) (0) (0)	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	(20) (0) (0)	(200) (0) (0) (0)
(Endocrine system)	stem)				
pituitary	angiectasis	$ \begin{array}{ccccccccccccccccccccccccccccccccc$	<50> 0 2 0 (0) (4) (0) (0)	<50> (0) (0) (0) (0)	<50> 0 1 0 (0) (2) (0) (0)
	cyst	4 4 0 0 (8) (8) (0) (0)	4 0 0 0 0 (8) (9) (0)	6 1 0 0 (12) (12) (13) (13) (13) (14)	3 0 0 0 (0) (9)
	hyperplasia	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	11 6 0 0 (22) (12) (0) (0)	5 6 0 0 (10) (12) (0) (0)	7 6 0 0 (14) (12) (0) (0)
	Rathke pouch	2 0 0 0 (4) (4) (6) (6) (6)	1 0 0 0 (2) (2) (3) (4) (4)	2 0 0 0 (4) (4) (6) (6) (6)	1 0 0 0 (2) (2) (3) (4)
thyroid	follicular hyperplasia	(0)(0)(0)(0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	<50> (0) (0) (0) (0) (0) (0) (0) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)
Grade 1: Slight (a > a: Number b b: Number (c) c: b/a* Significant difference;	1: Slight 2: Moderate 3: 1 a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100 lifference; *: P ≤ 0.05 **: P ≤ 0.	3 : Marked 4 : Severe site ≤ 0.01 Test of Chi Square			

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%) STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE

PAGE: 24 11 4 0 0 (22) (22) (8) (0) (0) 00 00 00 1 0 0 2) (0) (0 500 ppm 2 3 (%) (%) 0 0 0 0 0 0 0 0 10 3 0 (20) (6) (0) (1 (2) (-) - ;; - ;; - ;; 8 5 0 0 (16)(10)(0)(0) 2 3 4 (%) (%) (%) 00 00 00 0 0 00 250 ppm 5 2 0 (10) (4) (0) (0 1 0 (0) (0) (0) (0) (2)(2)(0)(3 0 0 6 6) (9) - 8 4 8 00 00 00 00 00 125 ppm 000 13 3 1 (26) (6) (2) (0 0 0 0 0 1 0 (0) (0) (0) (0) 2 3 (%) (%) $\overline{}$ 0 0 0 00 5 4 0 (10) (8) (0 • 6 20 ----2) (2 3 4 (%) (%) (%) 00 00 00 00 00 00 Control 0 1 0 (0) (2) (0) (13 3 0 (26) (6) (0) (0 0 0 0 8 4 0 (16) (8) (0) (1 0 0 (2) (2) (3) (3) (4) 0 0 0 0 4 : Severe Group Name No. of Animals on Study 3 : Marked 2 : Moderate focal fatty change:cortex hyperplasia:cortical cell peliosis-like lesion hyperplasia:medulla C-cell hyperplasia 1 : Slight Findings. {Reproductive system} cyst (Endocrine system) thyroid adrenal Organ Grade

BAIS4

Test of Chi Square

: P ≤ 0.01

Significant difference; *: P ≤ 0.05

(HPT150)

a : Number of animals examined at the site b : Number of animals with lesion c : b / a * 100

(a)

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS $(0{\text{--}}105\text{W})$

STUDY NO. : 056 ANIMAL : RAI REPORT TYPE : A1 SEX : FER	: 0560 : RAT F344/DuCrICrlj[F344/DuCrj] : A1 : FEMALE	HISTOP ALL AN	HISTOPATHOLOGICAL FINDINGS : ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)	JARY)	PAGE: 25
Organ	Findings	Group Name No. of Animals on Study Grade (%)	Control 50 3 4 (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%)	500 ppm 50 1 2 3 4 (%) (%) (%) (%)
{Reproductive system} uterus cysti	re system} cystic endometrial hyperplasia	5 (10)	<50> 2 0 0 0 (4) (0) (0)	<50> 4 0 0 (8) (0) (0) (0)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	(50) 6 1 0 0 (12) (2) (0) (0)
(Nervous system) brain	item} hemorrhage	0)	<50> 0 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	<50> 1 0 0 0 (2) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0
(Special sens eye	(Special sense organs/appendage) eye cataract	2 (4	<50> 2 1 0 0 4) (2) (0) (0)	<pre></pre>	<50> 0 4 0 0 (0) (8) (0) (0)	(50) 1 3 0 0 (2) (6) (0) (0)
	retinal atrophy	1 (2)	0 2 0) (4) (0)	0 0 1 2 (0) (0) (2) (4)	0 0 3 1 (0) (0) (6) (2)	0 0 3 1 (0) (0) (6) (2)
	keratitis	(0)	(0)(0)(0)(0		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	0 1 0 0 (0) (0) (0)
Grade <a>> b (c) Significant d	Grade 1 : Slight 2 : Moderate 3 : N < a > a : Number of animals examined at the site b : Number of animals with lesion (c) c : b / a * 100 Significant difference ; * : P \leq 0.05 ** : P \leq 0.05	farked 4: Sev	ere luare			

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%)

STUDY NO. : ANIMAL : REPORT TYPE : SEX :	: 0560 : RAT F344/DuCrlCrlj[F344/DuCrj] : Al : FEMALE	HISTOPATHOLOGICAL FINDINGS : ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105#)		PAGE: 26
Огвал	Findings	Group Name No. of Animals on Study Grade (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%)	250 ppm 50 1 2 3 4 (%) (%) (%) (%)	ł
{Special sense	(Special sense organs/appendage) bye degeneration:cornea	(50)	(50)	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<50> 1 0 0 0
Harder gl	degeneration	\$ \(\frac{1}{2} \) \(\frac{1} \) \(\frac{1} \) \(\frac{1}{2} \) \(\frac{1}{2} \	(20) (0)) (0) (0) 0 0 0 0 0 0 0 0 0) (0) (0) (20) (20)
	lymphocytic infiltration			2 0 0 0 (4) (4) (6) (6) (6)	
nasolacr d	inflammation	$\begin{pmatrix} <50 > & \\ 1 & 5 & 0 & 0 \\ (& 2) & (& 10) & (& 0) & (& 0) \end{pmatrix}$	<50> 0 5 0 0 (0) (10) (0) (0)	<50> 0 5 1 0 (0) (10) (2) (0)	<50> (0) (12) (0) (0)
(Musculoskeletal system)	al system)				
muscle	fibrosis	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	<pre></pre>	(0)(0)(0)(0) 0 0 0 0 0 0 0 0
ьопе	osteosclerosis	3 0 0 0 (9) (9) (9)	<50> 2 2 0 0 (4) (4) (0) (0)	<50> 3 2 2 0 (6) (4) (4) (0)	<50> 1 2 0 0 (2) (4) (0) (0)
Grade 1 : Slight <a>a> a : Number b b : Number (c) c : b/a a Significant difference;	2 : Moderate of animals examined at of animals with lesion 100 *: P ≤ 0.05 ***	3 : Marked 4 : Severe the site			

500 ppm 50 (%) 3 % - 8 2 3 4 (%) (%) (%) 250 ppm 50 - 8 HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0--105W)2 3 4 (%) (%) (%) 125 ppm 50 **-** 8 4 8 Control 50 2 3 (%) - 8 Group Name No. of Animals on Study Grade STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE Findings_ Organ

PAGE: 27

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(Body cavities)

peritoneum

peritoneum			<20>	<20>	<20>	<20>
	inflammation		0 0 0 0	0 0 1 0	0 0 0	0 0 0
			(0) (0) (0) (0)	(0)(0)(2)(0)	(0) (0) (0) (0)	
-	Military Control of the Control of t		A PARTY AND A PART	THE PROPERTY OF THE PROPERTY O		
Grade	1 : Slight 2 : Moderate 3 : Marked	3 : Marked	4 : Severe			
< a >	a : Number of animals examined at the site	at the site				
ρ	b : Number of animals with lesion	uo				
(°)	c:b/a*100					
Significa	Significant difference ; *: P \leq 0.05 **: P \leq 0.01 Test	**: P ≤ 0.01 Te	st of Chi Square			

BAIS4

TABLE 01

NEOPLASTIC LESIONS-INCIDENCE

AND STATISTICAL ANALYSIS: MALE

STUDY No. : 0560 ANIMAL : RAT F344/DuCr1 SEX : MALE	N RAT F344/DuCrlCrlj[F344/DuCrj] MALE	NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS	L ANALYSIS	PAGE	: 39
Group Name	Control	125 ppm	250 ppm	500 ррт	
,	SITE : subcutis TUMOR : fibroma				
Tumor rate Overall rates(a)	3/50(6.0)	1/50(2.0)	5/50(10.0)	6/50(10.0)	
Adjusted rates(b) Terminal rates(c)	7. 69 3/39(7. 7)	2.86 1/35(2.9)	9.76	5/37(13.5)	
Statistical analysis Peto test					
Standard method(d)	P = 0.3942				
<pre>// Prevalence method(d) Combined analysis(d)</pre>	P = 0.1098 $P = 0.1088$				
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.2232	P = 0.3087	P = 0, 3575	P = 0 3575	
	SITE : lung				
Tumor rate		enoma			
Overall rates(a)	2/50(4.0)	1/50(2.0)	3/50(6.0)	6/50(12.0)	
Adjusted rates(b) Terminal rates(c)	5. 13 2/39(-5. 1)	2.86 1/35(2 a)	6.98	15.00	
Statistical analysis			(6.E.) YE (7	0,01(10.0)	
Standard method(d)) =				
Prevalence method(d)	P = 0.0252*				
Cochran-Armitage test(e)	$F = \frac{1}{100}$ $P = 0.0441*$				
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.1343	
		,			
Tumor rate	TUMUK : bronchiolar-alveolar ade	bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma			
Overall rates(a)	3/50(6.0)	1/50(2.0)	5/50(10.0)	7/50(14.0)	
Adjusted rates(b) Terminal rates(c)	7. 69 3/39 (7. 7)	2.86 1/35(2.9)	11.63 4/41(9.8)	17. 50 6/37 (16. 2)	
Statistical analysis					
Standard method(d)	= d				
rrevalence method(d) Combined analysis(d)	F = 0.0292* P =				
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.0526	P = 0.3087	P = 0.3575	P = 0.1589	
(HPT360A)					

BAIS4

ANIMAL : RAT F344/Ducri	RAT F344/Ducrlcrlj[F344/Ducrj] MALE			
Group Name	Control	125 ppm	250 ppm	100 ppm
	SITE : spleen TUMOR : mononuclear cell leukemia			
Tumor rate Overall rates(a) Adjusted rates(b) Terminal rates(c)	7/50 (14. 0) 12. 82 5/39 (12. 8)	4/50(8.0) 5.71 2/35(5.7)	2/50(4.0) 2.44 1/41(2.4)	1/50(2.0) 0.0 0/37(0.0)
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	P = 0, 7385 P = 0, 9963 P = 0, 9916 P = 0, 0192*	P = 0, 2623	P = 0.0798	P = 0.0297*
	SITE : stomach TUMOR : squamous cell papilloma, squ	cell papilloma, squamous cell carcinoma		
Numor rate Overall rates(a) Adjusted rates(b) Terminal rates(c)	0/50(0.0) 0.0 0/39(0.0)	3/50(6.0) 6.00 2/35(5.7)	0/50(0.0) 0.0 0/41(0.0)	2/50(4.0) 4.88 1/37(2.7)
Statistical analysis Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.2412 P = 0.2412 P = P = P = 0.4908	P = 0.1212	P = N, C.	4.7
Tumor rate	SITE : liver TUMOR : hepatocellular adenoma			
Overall rates(a) Adjusted rates(b) Terminal rates(c) Statistical analysis	0/50(0.0) 0.0 0/39(0.0)	1/50(2. 0) 2. 86 1/35(2. 9)	3/50(6.0) 7.32 3/41(7.3)	3/50(6.0) 7.50 2/37(5.4)
reto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.0455* P = 0.0455* P = 0.0791	P = 0.5000	P = 0.1212	P = 0. 1212
(HPT360A)				

PAGE:

SITE liver	Control 125 ppm liver hepatocellular adenoma, hepatocellular carcinoma 0.0) 1/50(2.0) 2.86 0.0) 2.86	250 ppm	udd 009
SITE : TUMOR : TUMOR : TUMOR : TUMOR : Tumor 0/50 (ular adenoma, hepatocellular carcinoma 1/50(2.0) 2.86 1/35(2.9)		
tes(a) 0/50(ates(b) 0/39(analysis method(d) P = method(d) P = 0.04 analysis(d) P = itage test(e) P = 0.06 ct test(e) SITE : TUMOR : tes(b) 0/39(1/50(2.0) 2.86 1/35(2.9)		
analysis method(d)		4/50(8.0) 9.76 4/41(9.8)	3/50(6.0) 7.50 2/37(5.4)
SITE : TUMOR : tues(a) 1/50(P = 0.5000	P = 0.0587	
ites(a) 1/50(ates(b) 0/39(adenoma		
rates(c) 0/39(7/50(14.0)	2/50(4.0)	1/50(2.0)
l analysis	6/35(17.1)	2/41(4.9)	2.50 0/37(0.0)
Peto test Standard method(d) $P =$ Prevalence method(d) $P = 0.7934$ Combined analysis(d) $P =$ Cochran-Armitage test(e) $P = 0.3728$ Fisher Exact test(e)	P = 0.0297*	P = 0.5000	P = 0.7525
SITE : pancreas TUMOR : islet cell :	pancreas islet cell adenoma, islet cell adenocarcinoma		
	7/50(14 0)	3/50/ 6.0)	1/50(9 0)
ates(b) 1/39(17.50 6/35(17.1)	3/41(7.3)	2.50 (2.0) (0.0)
Statistical analysis Peto test Standard method(d) P = Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) P = 0.2648			
Fisher Exact test(e)	P = 0.0798	P = 0.5000	P = 0.5000

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OUTHER CONTRACTOR	190000	Action to the state of the stat			PAGE: 4
Group Name	Control	125 ppm	250 ppm	200 ppm	T TOTAL AND A STATE OF THE STAT
	SITE : pituitary gland TUMOR : adenoma				
lumor rate Overall rates(a)	12/50(24.0)	9/50(18.0)	9/50(18.0)	5/50(10.0)	
Adjusted rates(b) Terminal rates(c) Statistical analysis	17. 95 7/39 (17. 9)	15.38 4/35(11.4)	19.57 7/41(17.1)	7.32 2/37(5.4)	
Peto test Standard method(d)	D = 0.0169				
Prevalence method (d)	F = 0.9100 P = 0.8786 D = 0.0607				
Cochran-Armitage test(e)	P = 0.0730	1			
(a) again pygar (a)		F = 0.3121	P = 0.3121	P = 0.0542	
	SITE : thyroid TUMOR : C-cell adenoma				
lumor rate Overall rates(a)	7/50 (14.0)	11/50(22.0)	9/50(18.0)	6/50(12 0)	
Adjusted rates(b) Terminal rates(c)	17.95 7/39(17.9)	27. 78 9/35 (25. 7)	20. 45 8/41(19. 5)	5/37 (13.5)	
Statistical analysis Peto test					
Standard method(d) Prevalence method(d)	P = P = 0.7099				
Combined analysis(d) Cochran-Armitage test(e)	P = P = 0.5407				
Fisher Exact test(e)		P = 0.2178	P = 0.3929	P = 0.5000	
	SITE : thyroid TUMOR : C-cell carcinoma				The state of the s
Tumor rate Overall rates(a)	6/50(12.0)	1/50(2, 0)	3/50(6 0)	1/50(2 0)	
Adjusted rates(b)	5.13	2.86		0.00	
Statistical analysis	6/33(0.1)	1/35(2.9)	2/41(4.9)	0/37(0.0)	
Feto test Standard method(d) Prevalence method(d)	P = 0.8887 P = 0.8717				
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.9570 P = 0.0836	P = 0.0559	P = 0.2435	P = 0.0559	

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SITE : thyroid 125 ppm 125 ppm 250 ppm 250 ppm SITE : thyroid 12750 (24.0) 12750 (24.0) 7750 (7777				
SITE : thyroid 12/50(24.0) 12/50(25.0)	Group Name	Control	125 ррш	250 ppm	500 ppm	
12/50(26.0) 12/50(24.0) 12/50(24.0) 12/50(24.0) 12/50(24.0) 12/50(26.0) 12/50(26.0) 10/30(26.0) 10/30(26.0) 10/30(26.0) 10/30(26.0) 10/30(26.0) 10/30(26.0) 10/30(26.0) 10/30(26.0) 10/30(26.0) 10/30(26.0) 10/30(26.0) 10/30(26.0) 10/30(26.0) 10/30(26.0) 2/30(2			ll carcinoma			
P = 0.8887 P = 0.8887 10,98 (23. 1)	umor rate Overall rates(a)	13/50(26.0)	12/50 (24. 0)	12/50(24.0)	7/50/ 14 0)	
P = 0.8887 10/35 (28.6) 10/41 (24.4) 10/35 (28.6) 10/41 (24.4) 10/35 (28.6) 10/41 (24.4) 10/35 (28.6) 10/41 (24.4) 10/35 (28.6) 10/41 (24.4) 10/35 (28.6) 10/41 (24.4) 10/35 (28.6) 10/41 (24.4)	Adjusted rates(b)	23. 08	30.56	25.00	13.95	
st(a) P = 0.8887 P = 0.8825 st(b) P = 0.1335 P = 0.8255 P = 0.5000 P = 0.5000 P = 0.100 SITE : thyroid TUMOR : follicular adenoma, follicular adenocarcinoma O/50(0.0)	Terminal rates(c) tatistical analysis	9/39(23.1)	10/35(28.6)	10/41 (24. 4)	5/37(13.5)	
10 P = 0.855 11 P = 0.855 12 P = 0.49287 13 P = 0.49287 14 P = 0.1335 15 P = 0.49287 15 P = 0.1335 15 P = 0.1335 15 P = 0.1335 15 P = 0.219 15 P = 0.247 1	Peto test Standard method(d)	D = 0 8887				
1)	Prevalence method(d)	P = 0.8525				
SITE : thyroid TUMOR : follicular adenocarcinoma 0/50(0.0) 0/50(0.0) 0/50(0.0) 2/50(4.0) 2/50(6.0) 2/50(4.0) 2/50(6.0) 2/5	Combined analysis(d)	P = 0.9287				
SITE : thyroid TUMOR : follicular adenoracinoma 1500 (4.0) 2/500	cochran-Armitage lest(e) Fisher Exact test(e)	F = 0.1335	H	P = 0.5000		
0,50(0.0) 3,50(6.0) 2,50(4.0) 2,50(4.0) 2,50(4.0) 2,50(4.0) 2,50(4.0) 2,35(5.7) 2,35(5.7) 2,41(4.9) 2,37(follicular adenocarcinoma			
0,50(0,0)	mor rate					
December 1,14 4,88 2/37 2/36 5.7 2/41 4,9 2/37	verall rates(a)	0/50(0.0)	3/50(6.0)	2/50(4.0)		
D E C C C C C C C C C	djusted rates(b) erminal rates(c)	0.0				
P = 0.2219 P = 0.2219 SITE : adrenal gland TUMOR : pheochromocytoma 4/50(8.0) 1/50(2.0) 2/50(3.7(3.3) 1/30(3.4) 1/41(2.4) 2/37(3.3) 1/30(3.0) 1/41(3.4) 2/37(3.3) 1/30(3.0) 1/41(3.4)	atistical analysis					
1) P = 0.2219 P = 0.2475	ero test Standard method(d)					
1) P =	Prevalence method(d)	P = 0.2219				
SITE : adrenal gland TUMOR : pheochromocytoma 4/50(8.0) 4/50(8.0) 2/39(5.1) P = 0.1212 P = 0.2475 P = 0.244 P = 0.244 P = 0.2709 P = 0.6425 P = 0.1212 P = 0.2475 P = 0.247	Combined analysis(d)	P = C				
SITE : adrenal gland TUMOR : pheochromocytoma 4/50(8.0) 4/50(8.0) 2/50(2.0) 8.70 2/39(5.1) P = 1) P = 0.844 2/39(5.1) 2/30(2.0) 2/50(2.0) 2/44 2/39(5.1) 2/37(2/37(2/37(2/30) P = 0.2709 P = 0.2709 P = 0.6475 P = 0.1811	ochran-Armilage test(e) isher Exact test(e)	r = 0, 4/44	P = 0.1212	P = 0.2475		
SITE : adrenal gland TUMOR : pheochromocytoma 4/50(8.0) 4/50(8.0) 1/50(2.0) 2/50(2.44 2/39(5.1) 2/39(5.1) 3/35(8.6) 1/41(2.4) 2/37(1) P = 0.8442 1) P = 0.8442 1) P = 0.8442 3) Six (e) P = 0.2709 1) P = 0.2709						
$4/50(8.0) \qquad 4/50(8.0) \qquad 1/50(2.0) \qquad 2/50(8.0) \qquad 1/50(8.0) \qquad 1/50(8.0) \qquad 2/44 \qquad 2/39(8.0) \qquad 1/41(8.4) \qquad 1/41(8.4)$						
4/50(8.0) $4/50(8.0)$ $1/50(2.0)$ 2.70 2.70 $3/35(8.6)$ $1/41(2.4)$ $2/37($ $2/$	umor rate					
2/39(5.1)	Jverali rates(a) Adiusted rates(h)	4/50(8.0)	4/50(8.0)			
D =	Terminal rates(c)	2/39(5.1)	10.81			
method(d) P = method(d) P = 0.8442 analysis(d) P = analysis(e) P = 0.2709 ct fast(e) P = 0.2709 p = 0.6425 p = 0.1811	tatistical analysis					
P = 0.8442 P = P = 0.2709 P = 0.405 P = 0.405 P = 0.1811	eto test Standard method(d)					
P = $P = 0.2709$ $P = 0.405$ $P = 0.1811$	Prevalence method(d)					
V = 0.2(09) $P = 0.6405$ $P = 0.1811$	Combined analysis(d)	P =				
I = 0.01.10 - 1	ochran-Arminage lesi(e) Fisher Exact test(e)	r = 0.2709	P = 0.6425	P = 0.1811	P = 0.3389	

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STUDY No. : 0560 ANIMAL : RAT F344/Ducklcklj[F344/Duckj] SEX : MALE

Group Name	Control	125 ppm	250 ppm	200 mdd	
limov rate	SITE : adrenal gland TUMOR : pheochromocytoma:malignant	gnant			
numon rates (a) Overall rates (a) Adjusted rates (b) Terminal rates (c) Statistical analysis	0/50(0.0) 0.0 0/39(0.0)	1/50(2.0) 2.86 1/35(2.9)	3/50(6.0) 4.88 2/41(4.9)	0/50(0.0) 0.0 0/37(0.0)	
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	P = 0, 4074 P = 0, 5147 P = 0, 4826 P = 1, 0000	P = 0, 5000	P = 0.1212	P = N. C.	
	SITE : adrenal gland TUMOR : pheochromocytoma:	chromocytoma:malignant			
lumor rate Overall rates(a) Adjusted rates(b) Terminal rates(c)	4/50(8.0) 8.70 2/39(5.1)	5/50(10.0) 13.51 4/35(11.4)	4/50(8.0) 7.32 3/41(7.3)	2/50(4.0) 5.41 2/37(5.4)	
	P = 0.4074 P = 0.8223 P = 0.8008 P = 0.3406	P.= 0.5000	P = 0.6425	P = 0. 3389	
Tumor rate	SITE : testis TUMOR : interstitial cell tumor				
Overall rates(a) Adjusted rates(b) Terminal rates(c) Statistical analysis	42/50(84. 0) 94. 87 37/39(94. 9)	44/50(88. 0) 97. 37 34/35(97. 1)	46/50(92. 0) 97. 73 40/41(97. 6)	43/50(86.0) 97.50 36/37(97.3)	
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	P = P = 0.2809 P = P = 0.8003	P = 0.3871	P = 0.1783	P = 0.5000	

S	ANALYSIS
WEOPLASTIC LESIONS-INCIDENCE	TATISTICA
WEOPLASTIC LESIONS-INCIDENCE	AND
	WEOPLASTIC LESIONS-INCIDENCE

: 0560 : RAT F344/DuCrlJi[F344/DuCrJ] : MALE

STUDY No. ANIMAL SEX

Tumor rate Overall rates(a) Adjusted rates(b) Statistical analysis Peto test Standard method(d) P = 0.2456 Prevalence method(d) P = 0.2389 Combined analysis(d) P = 0.2456 Frisher Exact test(e) Tumor : adenoma	7 1	2/50(4.0) 4.88 2/41(4.9)	3/50(6.0) 5.41 2/37(5.4)	
1) 1) st(e)	2/50(2/50(4.0) 4.88 2/41(4.9)		
1/50(0/39(0/39(1) P = 0.245 1) P = 0.166 51(e) P = 0.329	2/50(2/50(4.0) 4.88 2/41(4.9)		
0/39(P = 0.245 P = 0.235 D = 0.166 St (e) P = 0.325	1/35(2/41(4.9)		
1) 1) st(e) s)				
fisher Exact test(e)				
	P = 0.5000	P = 0.5000	P = 0.3087	
STTR : hrain				AND
Tumor rate				
)02/0	3/50(6.0)	1/50(2.0)	1/50(2.0)	
		0.0		
Terminal rates(c) 0/39(0.0)	3/35(8.6)	0/41(0.0)	0/37(0,0)	
Statistical analysis				
Prevalence method(d) $P = 0.7956$				
Combined analysis(d) $P = 0.4569$				
Cochran-Armitage test(e) $P = 0.9390$				
Fisher Exact test(e)	P = 0.1212	P = 0.5000	P = 0.5000	

-----: There is no data which should be statistical analysis. Significant difference ; *: $P \le 0.05$ **: $P \le 0.01$ N.C.:Statistical value cannot be calculated and was not significant.

113

⁽a): Number of tumor-bearing animals/number of animals examined at the site.
(b): Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c): Observed tumor incidence at terminal kill.
(d): Beneath the control incidence are the P-values associated with the trend test.
Standard method : Death analysis
Prevalence method : Incidental tumor test
Combined analysis : Death analysis + Incidental tumor test

⁽e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
? The conditional probabilities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.

TABLE 02

NEOPLASTIC LESIONS-INCIDENCE

AND STATISTICAL ANALYSIS: FEMALE

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Group Name	Control	125 ppm	250 ppm	200 mbm	
	SITE : lung TUMOR : bronchiolar-alveolar	lung bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma			THE PARTY OF THE P
Tumor rate					
Overall rates(a)	1/50(2.0)	0/50(0.0)	1/50(2.0)	3/50(6 0)	
Adjusted rates(b)	2.33	0.0			
Terminal rates(c)	0/38(0.0)	0/43(0.0)	1/41(2.4)	3/37(8.1)	
Statistical analysis					
reto test					
Standard method(d)	1				
Tevalence method(d)	$\Gamma = 0.0395$				
Cochran-Armitage test(e)	P =				
Fisher Exact test(e)	1 - 0:1019	P = 0.5000	P = 0.7595	7306 O - Q	
			I = 0. (323	$\Gamma = 0.303$	
Timor rate	lumun . mononuclear cell leukemla	omia			
Overall rates(a)	5/50(10 0)	5/50(10 0)	(0 61 /02/3		
Adjusted rates(b)	7.89	6 98	0/30(12.0)	1/50(2.0)	
Terminal rates(c)	3/38(7 9)	3/43(7.0)	3,717 (7 3)	0.0	
Statistical analysis			(6:1) 11/6		
Peto test					
Standard method(d)	P = 0.6530				
Prevalence method(d)	P = 0.9415				
Combined analysis(d)	P = 0.9206				
Cochran-Armitage test(e)	p = 0 1336				
Fisher Exact test(e)	1 0:1000	P = 0.6297	P = 0.5000	P = 0 1022	
***************************************			***	77.7	
	TUMOR : adenoma				
lumor rate					
Overall rates(a)	13/50(26.0)	14/50 (28.0)	13/50 (26.0)	7/50 (14.0)	
Adjusted rates(b)	23. 68	27.91	26.83	16.22	
Terminal rates(c)	9/38(23.7)	12/43(27.9)	11/41 (26.8)	6/37 (16.2)	
Statistical analysis				î î	
Peto test					
Standard method(d)	P = 0.9002				
Prevalence method(d)	P = 0.8232				
Combined analysis(d)	P = 0.9256				
Cochean-Armitage test(e)	P = 0 1081				
Giot. C. Brost ++(-)	1001.0				
		D = 0 5000	D == 0 E000	D - 0 10EA	

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Group Name	Control	125 ppm	250 ppm	900 ppm
	SITE : pituitary gland TUMOR : adenoma,adenocarcinoma			
Tumor rate				
Overall rates(a) Adjusted rates(b)	14/50(28.0)	14/50(28.0)	13/50(26.0)	8/50(16.0)
Terminal rates(c) Statistical analysis	10/38 (26. 3)	27.91 12/43(27.9)	.26.83 11/41(26.8)	16. 22 6/37 (16. 2)
Standard method(d)	P = 0.7569			
Prevalence method(d)	P = 0.8733			
Cochran-Armitage test(e)	r = 0.9123 $P = 0.1264$			
Fisher Exact test(e)		P = 0.5880	P = 0.5000	P = 0.1135
	SITE : thyroid TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	6/50(12.0)	2/50(4.0)	3/50(-6.0)
Adjusted rates(b)	13.16	13.33		
Terminal rates(c)	5/38(13.2)	5/43(11.6)	2/41(4.9)	3/37(8.1)
odalistical analysis Peto test				
Standard method(d)	p =			
Prevalence method(d)	P = 0.8950			
Combined analysis(d)	P =			
Cochran-Armitage test(e)	P = 0.1840			
risher Exact test(e)		F = 0.6202	P = 0.1343	P = 0.2435
	SITE : thyroid TUMOR : C-cell adenoma, C-cell carcinoma	carcinoma		
Tumor rate	Š			
Overall rates(a)	(/50(14.0)	6/50(12.0)	2/50(4.0)	4/50(8.0)
Adjusted rates(b)	15.79	13.33	4.88	10.81
lerminal rates(c) Statistical analysis	6/38(15.8)	5/43(11.6)	2/41(4.9)	4/37(10.8)
Peto test Standard method(d)	□ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □			
Prevalence method(d)				
Combined analysis(d)	Ш			
	P = 0.2372			
Dishow Dunct +cont(c)				

ANALYSIS
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NEOPLASTIC

STUDY No. : 0560 ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj] SEX : FEMALE

Group Name	Control	125 ppm	250 ррш	200 ppm	
	SITE : uterus TUMOR : endometrial stromal polyp				
lumor rate Overall rates(a) Adjusted rates(b)	5/50(10.0) 13.16	3/50(6.0) 6.98	5/50(10.0)	3/50(6.0)	
Terminal rates(c) Statistical analysis	5/38(13.2)	3/43(7.0)	4/41(9.8)	3/37(8.1)	
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	P =	P = 0.3575	P = 0.6297	P = 0.3575	
	SITE : uterus TUMOR : endometrial stromal sarcoma				
Tumor rate Overall rates(a)	3/50(6.0)	1/50(2.0)	1/50(2.0)	3/50(6.0)	
Terminal rates(c) Statistical analysis	0/38(0.0)	0/43(0.0)	2.27 0/41(0.0)	2. 13 0/37(0.0)	
Standard method(d) Prevalence method(d) Combined analysis(d)	P = 0.6383 P = 0.1356 P = 0.3917				
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.8073	P = 0.3087	P = 0.3087	P = 0.6611	
·	SITE : mammary gland TUMOR : fibroadenoma				
Overall rates(a)	8/50 (16.0)	5/50 (10.0)	5/50(10.0)	1/50(2.0)	
Adjusted rates(b) Terminal rates(c) Statistical analysis	18.42 7/38 (18.4)	11. 63 5/43 (11. 6)	10.00 3/41(7.3)	0.0 0/37(0.0)	
Standard method(d) Prevalence method(d) Combined analysis(d)	P = 0, 3865 P = 0, 9958 P = 0, 9907				
Coolingii Allinidage (est (e) Fisher Exact (est (e)		P = 0.2768	8926 0 - 0	4610 0 - 0	

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

STUDY No.

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

: RAT F344/DuCrlCrlj[F344/DuCrj] : FEMALE

STUDY No. ANIMAL SEX

ora · remale				P P	PAGE : 12
Group Name	Control	125 ppm	250 ppm	200 mad	
Tumor rate Overall rates(a) Adjusted rates(b) Terminal rates(c) Statistical analysis Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	SITE : preputial/clitoral gland TUMOR : adenoma 2/50(4.0) 5.26 2/38(5.3) P = 0.1474 P = 0.5361 P = 0.3365 P = 0.7508	4/50(8.0) 9.09 3/43(7.0) P = 0.3389	6/50(12.0) 9.76 4/41(9.8) P = 0.1343	3/50(6.0) 5.41 2/37(5.4)	
(HPT360A)					BAIS4

(a): Number of tumor-bearing animals/number of animals examined at the site.
(b): Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c): Observed tumor incidence at terminal kill.
(d): Beneath the control incidence are the P-values associated with the trend test.
Standard method : Death analysis
Prevalence method : Incidental tumor test

BAIS4

Combined analysis: Death analysis + Incidental tumor test

(e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.

?: The conditional probabilities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.

-----: There is no data which should be statistical analysis.

Significant difference; *: P ≤ 0.05 **: P ≤ 0.01

N.C.:Statistical value cannot be calculated and was not significant.

TABLE Q

HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : $F344/DuCrlCrlj\ MALE\ RATS$

TABLE Q HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER: F344/DuCrlCrlj MALE RATS

Organs	No. of animals	No. of animals	Incidence	Min Max.
Tumors	examined	bearing tumor	(%)	(%)
Lung	2199			
Bronchio-alveolar adenoma 1)		84	3.8	0 - 12
Bronchio-alveolar carcinoma 2)		19	0.9	0 - 8
1)+2)		103	4.7	0 - 14
Liver	2199			
Hepatocellular adenoma 1)		41	1.9	0 - 8
Hepatocellular carcinoma 2)		7	0.3	0 - 2
1)+2)		47	2.1	0 - 8
Pncreas	2199			
Islet cell adenoma		46	2.1	0 - 14

Forty four carcinogenicity studies examined in Japan Bioassay Research Center were used.

Study No.: 0043, 0059, 0061, 0063, 0065, 0067, 0095, 0104, 0115, 0130, 0141, 0158, 0162, 0189, 0205, 0210, 0224, 0242, 0246, 0267, 0269, 0278, 0284, 0288, 0294, 0296, 0318, 0328,

 $0342,\,0347,\,0365,\,0371,\,0396,\,0399,\,0401,\,0407,\,0417,\,0421,\,0437,\,0448,\,0457,\,0461,\,0427,\,0421,\,0437,\,0448,\,0457,\,0461,\,0467,\,0467$

0497, 0535

TABLE R

CAUSE OF DEATH OF RATS IN THE 2-YEAR INHALATION STUDY OF 1 - BROMOBUTANE

TABLE R CAUSE OF DEATH OF RATS IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

		М	ale			Fer	nale	
Group name	Control	125 ppm	250 ppm	500 ppm	Control	125 ppm	250 ppm	500 ppm
Number of dead or moribund animals	11	15	9	13	12	7	9	13
Urinary system lesion	0	2	0	0	0	0	0	0
Chronic nephropathy	0	0	0	1	0	0	0	0
Peritonitis	0	0	0	0	0	1	0	0
Tumor death : leukemia	2	2	1	1	2	2	3	1
skin / appendage	0	1	1	0	0	0	0	0
subcutis	0	1	1	1	0	0	0	0
lymph node	0	0	0	0	1	0	0	0
spleen	0	0	0	1	0	0	0	0
kidney	0	1	0	0	0	0	0	0
urinary bladder	0	0.	0	0	0	0	0	1
pituitary gland	5	3	0	2	4	2	2	2
thyroid	4	0	1	1	0	0	0	0
adrenal gland	0	0	1	0	0	0	0	0
uterus	_	_	******	_	3	1	0	2
mammary gland	0	0	0	0	1	0	0	2
preputial/clitoral gland	0	1	0	1	0	0	2	1
brain	0	0	2	1	0	0	0	0
Zymbal gland	0	1	1	2	0	0	1	2
vertebra	N-water	_	_	accesses.	0	0	0	1
bone	0	2	0	0	0	0	0	0
No microscopical confirmation	0	1	1	2	1	1	1	1

FIGURES

FIGURE 1	1 - BROMOBUTANE VAPOR GENERATION SYSTEM AND INHALATION SYSTEM
FIGURE 2	SURVIVAL ANIMAL RATE OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF 1 - BROMOBUTANE
FIGURE 3	SURVIVAL ANIMAL RATE OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF 1 - BROMOBUTANE
FIGURE 4	BODY WEIGHT CHANGES OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF 1 - BROMOBUTANE
FIGURE 5	BODY WEIGHT CHANGES OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF 1 - BROMOBUTANE
FIGURE 6	FOOD CONSUMPTION CHANGES OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF 1 - BROMOBUTANE
FIGURE 7	FOOD CONSUMPTION CHANGES OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF 1 - BROMOBUTANE

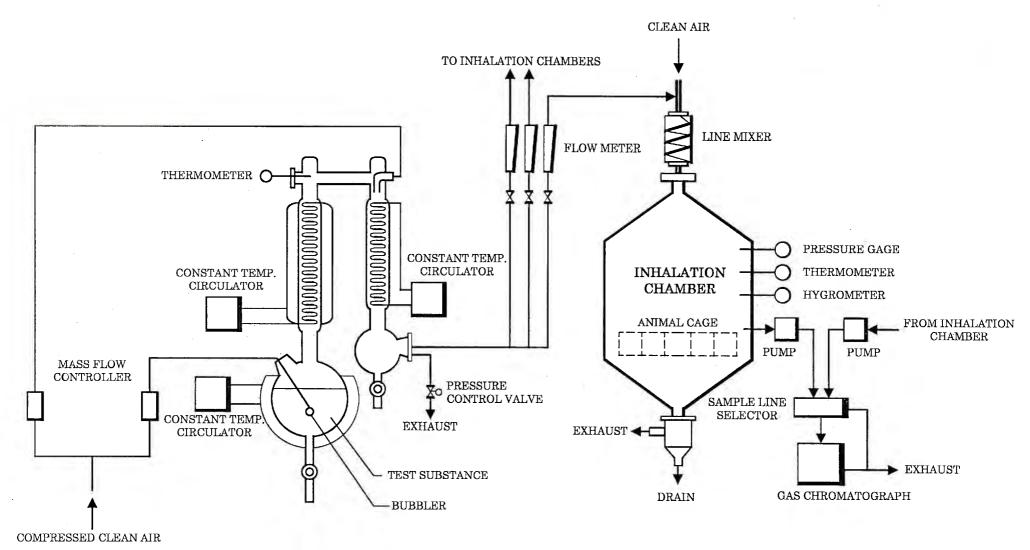


FIGURE 1 1-BROMOBUTANE VAPOR GENERATION SYSTEM AND INHALATION SYSTEM

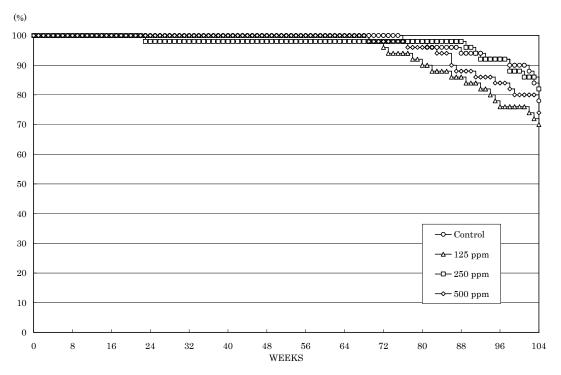


FIGURE 2 SURVIVAL ANIMAL RATE OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

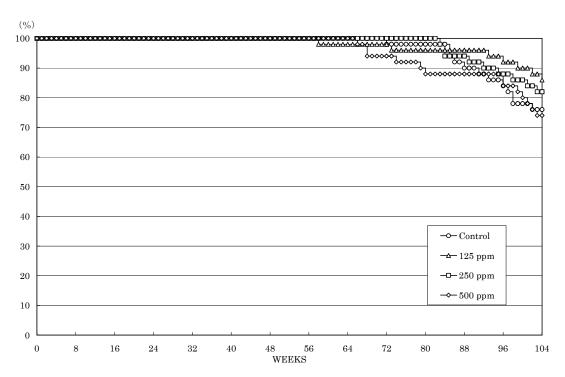


FIGURE 3 SURVIVAL ANIMAL RATE OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

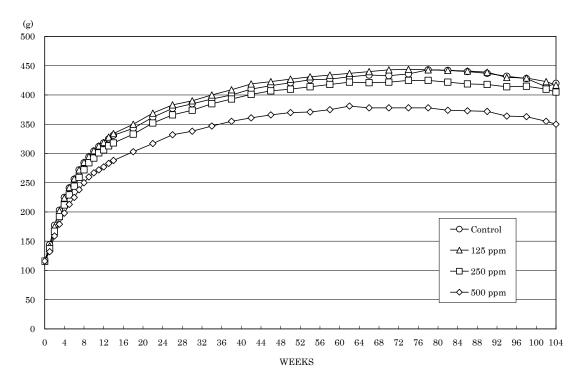


FIGURE 4 BODY WEIGHT CHANGES OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

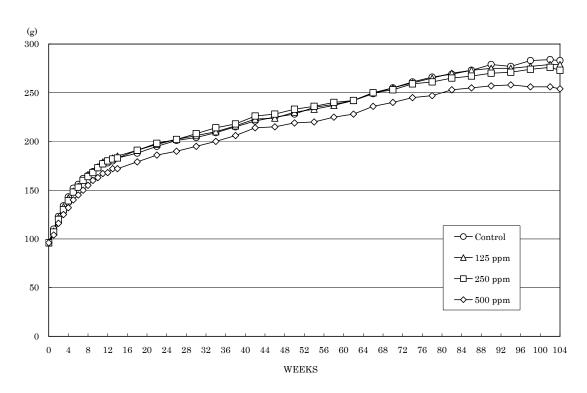


FIGURE 5 BODY WEIGHT CHANGES OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

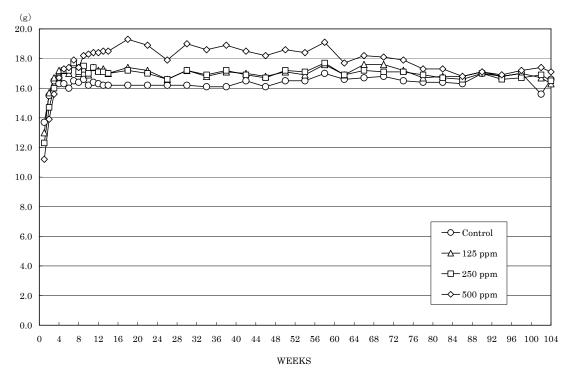


FIGURE 6 FOOD CONSUMPTION CHANGES OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

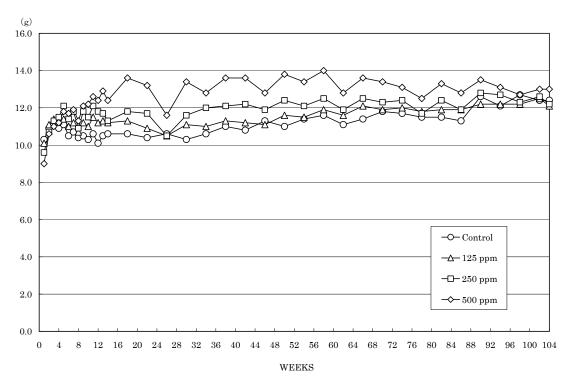


FIGURE 7 FOOD CONSUMPTION CHANGES OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE