塩化メチルのラット及びマウスを用いた吸入によるがん原性予備試験報告書

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APPENDIX B 1-1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS · _ _ _

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SEX : MALE

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PAGE: 1

linical sign	Group Name		stration We												
		0-0	1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
		1	1	1	1	1	1	1	1	1	1	1	1		1
OCOMOTOR MOVEMENT DECR	0 ppm	0	0	0	0	0	0	C	0	0	0	0	0	0	0
	190 ppm	0	0	0	0	0	0	Ō	0	0	0	0	0	0	0
	380 ppm	0	0	0	0	0	0	0	0	0	0	Ö	Ō	Ō	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	0
ATERAL	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	190 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	380 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	0
ASTING	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	190 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	380 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	0
ILOERECTION	maa 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	190 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	380 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	0
XOPHTHALMOS	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	190 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	380 ppm	- 0	0	1	1	1	1	1	1	1	1	1	1	1	1
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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CLINICAL	OBSERVATION	(SUMMARY)
ALL ANIM	ALS .	

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Clinical sign	Group Name	A alas i sa i		[]					• • • • • • • • • •						
ormoar sign	or oup mane	0-0	stration We 1-7	зек-аау 2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11 0	10.7	10.7
		1	1	1	1	4-7 1	1	1	1	1	9-7 1	10-7	11-7 1	12-7 1	13-7 1
EYE OPACITY	mqq 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	190 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	380 ppm	0	1	1	1	1	1	1	1	1	1	1	1	1	1
	750 ppm	0	1	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	. 0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CORNEAL OPACITY	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	190 ppm	0	0	Ō	Õ	Ő	Ő	õ	0 0	õ	õ	0	0	0	0
	380 ppm	0	1	1	1	1	1	1	1	1	1	1	1	1	1
	750 ppm	0	0	0	ō	Ō	Ô	Ō	Ô	Ô	0	Ô	Ô	Ō	0
	1500 ppm	Ó	0	Õ	Õ	õ	Õ	Õ	0	õ	Ő	0	Ő	0	õ
	3000 ppm	0	0	0	0	Ő	Ő	Ő	Ő	Õ	Ő	0	0 0	0	Õ
ANTERIOS CHAMBER OPACITY	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	<u>^</u>	•
	190 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	380 ppm	0	õ	0	0	0	0	0	0	-	0	Ū	0	0	0
	750 ppm	0	1	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
									-	-	·	•	0	· ·	Ŷ
IRREGULAR BREATHING	mqq 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	190 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	380 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	0
ABNORMAL RESPIRATION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	190 ppm	0	0	0	0	0	Ō	0	Ō	Ő	õ	Õ	Õ	Ő	õ
	380 ppm	0	0	0	. 0	Ō	Õ	Õ	Õ	0	Ô	Õ	Ô	0	õ
	750 ppm	0	0	0	0	Ő	Õ	õ	õ	õ	õ	õ	õ	Ő	0
•	1500 ppm	0	0	0	0	Ō	Ō	Õ	0	0 0	õ	õ	Ô	0 0	0 0
	3000 ppm	0	0	0	0	Õ	Õ	õ	Ő	Û.	0 0	Õ	0	1	0

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SEX : MALE

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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PAGE : 3

Clinical sign	Group Name	Admini	stration We	eek-day											
		0-0	1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
· · · · · · · · · · · · · · · · · · ·		1	1	1	1	1	1	1	1	1	1	1	1	1	1
SUBNORMAL TEMP	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	190 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	380 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	0

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APPENDIX B 1-2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : FEMALE

PAGE: 4

Clinical sign	Group Name	Admini	stration W	eek-day											
		0-0 1	1-7 1	2-7 1	3-7 1	4-7 1	5-7 1	6-7 1	7-7 1	8-7 1	9–7 1	10-7	11-7	12-7 1	13-7 1
· · · · · · · · · · · · · · · · · · ·															
SOILED PERI GENITALIA	mqq 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	190 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	380 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	1	1	1	1	0	0	0	0	0	0	0
	3000 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	0

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APPENDIX B 1-3

CLINICAL OBSERVATION : SUMMARY, MOSUE : MALE

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 13

SEX : MALE

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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linical sign	Group Name	Admini	stration W	əek-day											
		0-0 1	1-7 1	2-7 1	3-7 1	4-7 1	5-7 1	6–7 1	7–7 1	8-7 1	9-7 1	10-7 1	11-7 1	12-7 1	13-7 1
UNCHBACK POSITION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	300 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	440 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	670 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	1	0	0	0	0	-	-	-	-
ILOERECTION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	300 ppm	0	0	0	0	0	0	0	0	. 0	0	0	0	0	0
	440 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	670 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	1	0	0	0	0	-	-	-	-
REGULAR BREATHING	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	300 ppm	0	0	0	0	0	0	0	0	0	Ó	Ó	0	0	Ō
	440 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	670 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	0	0	0	0	0	õ	Ő	0	õ	õ	0	0
	1500 ppm	0	0	0	0	0	1	0	0	0	0	-	-	-	-
BNORMAL RESPIRATION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	300 ppm	Ō	0	0	0	Ő	0	Ő	0	0	Ő	0	Ő	Ő	Ő
	440 ppm	0	Ő	Õ	õ	õ	Ô	õ	0 0	Õ	õ	õ	Õ	0	õ
	670 ppm	õ	Õ	õ	õ	õ	ñ	Õ	õ	0	Ň	ů N	Ň	0	Ň
	1000 ppm	Ő	0	0	0	ŏ	0	0	õ	0	õ	0	0	0	0
	1500 ppm	õ	0	0	0	0	1	0	0	0	0	-	v	v	~

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APPENDIX B 1-4

CLINICAL OBSERVATION : SUMMARY, MOSUE: FEMALE

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : FEMALE

PAGE : 2

Clinical sign	Group Name	Admini	stration We	eek-day											
		0-0	1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
RREGULAR BREATHING	mqq 0	0	٥	0	0	0	0	0	0	٥	0	٥	٥	0	٥
MEGGEAR DELATITING	300 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	440 ppm	0	0	0	0	0	0	0	0	0	ů.	0	0	0	0
	670 ppm	õ	ů 0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	õ	õ	õ	Ő	ů 0	õ	0	0	ů 0	0	0	0	0 0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	1	-	-	-
BNORMAL RESPIRATION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	300 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	440 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	670 ppm	0	0	0	0	0	0	0	0	0	0.	0	0	0	0
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	1	-	-	-

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APPENDIX B 2-1

BODY WEIGHT CHANGES :SUMMARY, RAT : MALE

BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

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STUDY NO. : 0191 ANIMAL : RAT F344 UNIT : g REPORT TYPE : A1 13 SEX : MALE

oup Name	Admini	stratio	n week-day											
	0-0		1-7		2-7		3-7		4-7		5-7		6-7	
0 popm	127±	5	158±	7	192±	8	213±	9	$231\pm$	10	249±	11	261±	11
190 ppm	127±	6	157±	9	185±	13	205±	13	225±	15	249±	15	$262\pm$	16
380 ppm	128±	6	154±	10	183±	11	202±	14	219±	15	$237\pm$	16	247±	17
750 ppm	127±	4	$153\pm$	6	178±	8*	$195\pm$	8**	206±	<u>9</u> **	$217\pm$	10**	$222\pm$	12**
1500 ppm	127±	6	$146\pm$	9*	$165\pm$	7**	179±	8**	186±	7**	$191\pm$	8**	$191\pm$	9**
3000 ppm	126±	5	133±	9**	$130\pm$	12**	$145\pm$	13**	$139\pm$	12**	$139\pm$	13**	139±	13**
Significant differer	nce; *:P≦0	.05	** : P ≦ 0.0)1			Test of D	unnett						
1260)														E

BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS -----

STUDY NO.: 0191 ANIMAL : RAT F344 UNIT : g REPORT TYPE : A1 13 SEX : MALE

up Name	Admin	istratio	n week-day											
	7-7		8-7		9–7		10-7		11-7		12-7		13-7	
0 ppm	272±	14	285±	15	299±	18	306±	18	317±	19	$325\pm$	20	335±	20
190 ppm	272±	19	284±	20	302±	21	310±	20	318±	21	323±	20	330±	21
380 maa	$257\pm$	18	$267\pm$	22	280±	27	$287\pm$	25	297±	24	303±	22	310±	21*
750 ppm	$227\pm$	15**	232±	15**	$241\pm$	15**	246±	15**	254±	14**	$260\pm$	15**	266±	14**
1500 ppm	$190\pm$	8**	$190\pm$	10**	195±	14**	195±	15**	199±	18**	203±	20**	210±	20**
3000 ppm	138±	12**	138±	14**	$144\pm$	17**	143±	17**	144±	15**	139±	19**	145±	17**
Significant difference	; *:P≦	0.05	** : P ≦ 0.	01			Test of Du	unnett						
(260)											<u></u>		<u>.</u>	

APPENDIX B 2-2

BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

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STUDY NO. : 0191 ANIMAL : RAT F344 UNIT : g REPORT TYPE : A1 13 SEX : FEMALE

Admini	stratio	n week-day											
0-0		1-7		2-7		3-7		4-7		5-7		6-7	
102±	3	117±	5	134±	4	140±	4	151±	5	160±	4	166±	6
103±	3	118±	4	130±	6	139±	8	$147\pm$	8	$158\pm$	10	164±	10
103±	3	118±	5	130±	6	137±	6	146±	7	156±	9	159±	9
102±	3	$116\pm$	5	126±	5*	$132\pm$	7*	138±	7**	146±	9**	148±	9 * *
$102\pm$	3	$112\pm$	4	120±	6**	$127\pm$	5**	130±	5**	$134\pm$	6**	134±	7**
102土	2	102±	4**	97±	8**	105±	7**	99±	7**	99±	9**	99±	8**
; *:P≦0	.05	**:P≦0.(Test of Du	Innett						
-	0-0 $102\pm$ $103\pm$ $103\pm$ $102\pm$ $102\pm$ $102\pm$	$\begin{array}{c cccc} 0 - 0 \\ \hline 102 \pm & 3 \\ 103 \pm & 3 \\ 103 \pm & 3 \\ 102 \pm & 3 \\ 102 \pm & 3 \\ 102 \pm & 2 \end{array}$	$102\pm$ 3 $117\pm$ $103\pm$ 3 $118\pm$ $103\pm$ 3 $118\pm$ $102\pm$ 3 $116\pm$ $102\pm$ 3 $112\pm$ $102\pm$ 2 $102\pm$	$0-0$ $1-7$ $102\pm$ 3 $117\pm$ 5 $103\pm$ 3 $118\pm$ 4 $103\pm$ 3 $118\pm$ 5 $102\pm$ 3 $116\pm$ 5 $102\pm$ 3 $112\pm$ 4 $102\pm$ 2 $102\pm$ $4**$	$0-0$ $1-7$ $2-7$ $102\pm$ 3 $117\pm$ 5 $134\pm$ $103\pm$ 3 $118\pm$ 4 $130\pm$ $103\pm$ 3 $118\pm$ 4 $130\pm$ $103\pm$ 3 $118\pm$ 5 $130\pm$ $102\pm$ 3 $116\pm$ 5 $126\pm$ $102\pm$ 3 $112\pm$ 4 $120\pm$ $102\pm$ 2 $102\pm$ $4**$ $97\pm$	$0-0$ $1-7$ $2-7$ $102\pm$ 3 $117\pm$ 5 $134\pm$ 4 $103\pm$ 3 $118\pm$ 4 $130\pm$ 6 $103\pm$ 3 $118\pm$ 5 $130\pm$ 6 $103\pm$ 3 $118\pm$ 5 $130\pm$ 6 $102\pm$ 3 $116\pm$ 5 $126\pm$ 5* $102\pm$ 3 $112\pm$ 4 $120\pm$ 6*** $102\pm$ 2 $102\pm$ 4*** $97\pm$ 8***	$0-0$ $1-7$ $2-7$ $3-7$ $102\pm$ 3 $117\pm$ 5 $134\pm$ 4 $140\pm$ $103\pm$ 3 $118\pm$ 4 $130\pm$ 6 $139\pm$ $103\pm$ 3 $118\pm$ 5 $130\pm$ 6 $139\pm$ $103\pm$ 3 $118\pm$ 5 $130\pm$ 6 $137\pm$ $102\pm$ 3 $116\pm$ 5 $126\pm$ $5*$ $132\pm$ $102\pm$ 3 $112\pm$ 4 $120\pm$ $6**$ $127\pm$ $102\pm$ 2 $102\pm$ $4**$ $97\pm$ $8**$ $105\pm$	$0-0$ $1-7$ $2-7$ $3-7$ $102\pm$ 3 $117\pm$ 5 $134\pm$ 4 $140\pm$ 4 $103\pm$ 3 $118\pm$ 4 $130\pm$ 6 $139\pm$ 8 $103\pm$ 3 $118\pm$ 5 $130\pm$ 6 $137\pm$ 6 $102\pm$ 3 $116\pm$ 5 $126\pm$ $5*$ $132\pm$ $7*$ $102\pm$ 3 $112\pm$ 4 $120\pm$ $6**$ $127\pm$ $5**$ $102\pm$ 3 $112\pm$ 4 $120\pm$ $6**$ $127\pm$ $5**$ $102\pm$ 2 $102\pm$ $4**$ $97\pm$ $8**$ $105\pm$ $7**$	$0-0$ $1-7$ $2-7$ $3-7$ $4-7$ $102\pm$ 3 $117\pm$ 5 $134\pm$ 4 $140\pm$ 4 $151\pm$ $103\pm$ 3 $118\pm$ 4 $130\pm$ 6 $139\pm$ 8 $147\pm$ $103\pm$ 3 $118\pm$ 4 $130\pm$ 6 $139\pm$ 8 $147\pm$ $103\pm$ 3 $118\pm$ 5 $130\pm$ 6 $137\pm$ 6 $146\pm$ $102\pm$ 3 $116\pm$ 5 $126\pm$ $5*$ $132\pm$ $7*$ $138\pm$ $102\pm$ 3 $112\pm$ 4 $120\pm$ $6**$ $127\pm$ $5**$ $130\pm$ $102\pm$ 2 $102\pm$ $4**$ $97\pm$ $8**$ $105\pm$ $7**$ $99\pm$	$0-0$ $1-7$ $2-7$ $3-7$ $4-7$ $102\pm$ 3 $117\pm$ 5 $134\pm$ 4 $140\pm$ 4 $151\pm$ 5 $103\pm$ 3 $118\pm$ 4 $130\pm$ 6 $139\pm$ 8 $147\pm$ 8 $103\pm$ 3 $118\pm$ 5 $130\pm$ 6 $139\pm$ 8 $147\pm$ 8 $103\pm$ 3 $118\pm$ 5 $130\pm$ 6 $137\pm$ 6 $146\pm$ 7 $102\pm$ 3 $116\pm$ 5 $126\pm$ $5*$ $132\pm$ $7*$ $138\pm$ $7**$ $102\pm$ 3 $112\pm$ 4 $120\pm$ $6**$ $127\pm$ $5**$ $130\pm$ $5**$ $102\pm$ 2 $102\pm$ $4**$ $97\pm$ $8**$ $105\pm$ $7**$ $99\pm$ $7**$	$0-0$ $1-7$ $2-7$ $3-7$ $4-7$ $5-7$ $102\pm$ 3 $117\pm$ 5 $134\pm$ 4 $140\pm$ 4 $151\pm$ 5 $160\pm$ $103\pm$ 3 $118\pm$ 4 $130\pm$ 6 $139\pm$ 8 $147\pm$ 8 $158\pm$ $103\pm$ 3 $118\pm$ 4 $130\pm$ 6 $139\pm$ 8 $147\pm$ 8 $158\pm$ $103\pm$ 3 $118\pm$ 5 $130\pm$ 6 $137\pm$ 6 $146\pm$ 7 $156\pm$ $102\pm$ 3 $116\pm$ 5 $126\pm$ $5*$ $132\pm$ $7*$ $138\pm$ $7**$ $146\pm$ $102\pm$ 3 $112\pm$ 4 $120\pm$ $6***$ $127\pm$ $5***$ $130\pm$ $5***$ $134\pm$ $102\pm$ 2 $102\pm$ $4***$ $87\pm$ $105\pm$ $7***$ $99\pm$ $7***$ $99\pm$	$0-0$ $1-7$ $2-7$ $3-7$ $4-7$ $5-7$ $102\pm$ 3 $117\pm$ 5 $134\pm$ 4 $140\pm$ 4 $151\pm$ 5 $160\pm$ 4 $103\pm$ 3 $118\pm$ 4 $130\pm$ 6 $139\pm$ 8 $147\pm$ 8 $158\pm$ 10 $103\pm$ 3 $118\pm$ 5 $130\pm$ 6 $137\pm$ 6 $146\pm$ 7 $156\pm$ 9 $102\pm$ 3 $116\pm$ 5 $126\pm$ $5*$ $132\pm$ $7*$ $138\pm$ $7**$ $146\pm$ $9***$ $102\pm$ 3 $112\pm$ 4 $120\pm$ $6***$ $127\pm$ $5***$ $134\pm$ $6***$ $102\pm$ 3 $112\pm$ 4 $120\pm$ $6***$ $127\pm$ $5***$ $134\pm$ $6***$ $102\pm$ 2 $102\pm$ $4***$ $97\pm$ $8**$ $105\pm$ $7***$ $99\pm$ $9***$ <td>$0-0$ $1-7$ $2-7$ $3-7$ $4-7$ $5-7$ $6-7$ $102\pm$ 3 $117\pm$ 5 $134\pm$ 4 $140\pm$ 4 $151\pm$ 5 $160\pm$ 4 $166\pm$ $103\pm$ 3 $118\pm$ 4 $130\pm$ 6 $139\pm$ 8 $147\pm$ 8 $158\pm$ 10 $164\pm$ $103\pm$ 3 $118\pm$ 5 $130\pm$ 6 $137\pm$ 6 $146\pm$ 7 $156\pm$ 9 $159\pm$ $102\pm$ 3 $116\pm$ 5 $126\pm$ $5*$ $132\pm$ $7*$ $138\pm$ $7**$ $146\pm$ $9**$ $148\pm$ $102\pm$ 3 $112\pm$ 4 $120\pm$ $6**$ $127\pm$ $5**$ $130\pm$ $5**$ $134\pm$ $6**$ $134\pm$ $102\pm$ 3 $112\pm$ 4 $120\pm$ $6**$ $127\pm$ $5**$ $134\pm$ $6**$ $134\pm$ $102\pm$ 2</td>	$0-0$ $1-7$ $2-7$ $3-7$ $4-7$ $5-7$ $6-7$ $102\pm$ 3 $117\pm$ 5 $134\pm$ 4 $140\pm$ 4 $151\pm$ 5 $160\pm$ 4 $166\pm$ $103\pm$ 3 $118\pm$ 4 $130\pm$ 6 $139\pm$ 8 $147\pm$ 8 $158\pm$ 10 $164\pm$ $103\pm$ 3 $118\pm$ 5 $130\pm$ 6 $137\pm$ 6 $146\pm$ 7 $156\pm$ 9 $159\pm$ $102\pm$ 3 $116\pm$ 5 $126\pm$ $5*$ $132\pm$ $7*$ $138\pm$ $7**$ $146\pm$ $9**$ $148\pm$ $102\pm$ 3 $112\pm$ 4 $120\pm$ $6**$ $127\pm$ $5**$ $130\pm$ $5**$ $134\pm$ $6**$ $134\pm$ $102\pm$ 3 $112\pm$ 4 $120\pm$ $6**$ $127\pm$ $5**$ $134\pm$ $6**$ $134\pm$ $102\pm$ 2

BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS ~~

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STUDY NO. : 0191 ANIMAL : RAT F344 UNIT : g REPORT TYPE : A1 13 SEX : FEMALE

oup Name	Admin	istration	n week-day											
	7-7		8-7		9-7		10-7		11-7		12-7		13-7	
maa 0	169±	6	172±	7	177±	8	180±	8	182±	8	186±	9	189±	9
190 mad	168±	11	172±	11	178±	11	180±	11	184±	12	188±	13	192±	11
380 ppm	163±	8	167±	8	171±	9	172±	11	177±	10	180±	11	181±	12
750 ppm	$150\pm$	8**	154±	8**	$156\pm$	10**	157±	11**	$162\pm$	9**	163±	9**	166±	9**
1500 ppm	$134\pm$	8**	$132\pm$	9**	$136\pm$	10**	135±	11**	136±	11**	$137\pm$	11**	$138\pm$	10**
3000 mag	100±	10**	98±	8**	100±	8**	98±	9**	99±	7**	98±	7**	99±	6**
Significant differe	ence; *:P≦	0.05	** : P ≤ 0.(01			Test of Du	unnett						
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APPENDIX B 2-3

BODY WEIGHT CHANGES :SUMMARY, MOSUE : MALE

BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS -----

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 UNIT : g REPORT TYPE : A1 13 SEX : MALE

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up Name	Administrati	on week-day					
	0-0	1-7	2-7	3-7	4-7	5-7	6–7
0 ppm	23.3± 0.9	25.2± 0.7	26.1± 1.0	27.0± 0.8	27.8± 1.0	29.3± 1.2	30.3± 1.5
300 ppm	23.1± 0.9	25.0± 0.8	25.5 ± 1.1	26.2± 1.1	26.5± 1.2*	27.3± 1.1**	27.5± 1.1**
440 ppm	23.2± 1.0	24.9± 1.1	25.2± 1.5	25.8± 1.2*	26.2± 1.3*	26.7± 1.3**	27.2± 1.3**
670 ppm	23.5 ± 1.2	24.4± 1.4	24.8± 1.3*	25.1± 1.3**	25.2± 1.3**	25.6± 1.4**	25.8± 1.2**
1000 ppm	23.1± 0.8	23.4± 0.8**	23.9± 0.6**	24.2± 0.8**	24.3± 0.5**	24.6± 0.6**	24.7土 0.6**
1500 ppm	23.3± 0.9	22.9± 0.9**	22.5± 0.6**	23.4± 1.1**	23.2± 1.1**	22.7± 2.3**	24.4± 1.1**
Significant difference ;	*:P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett			
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BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS ·____.

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STUDY NO. : 0192 ANIMAL : MOUSE BDF1 UNIT : g REPORT TYPE : A1 13 SEX : MALE

up Name	Administration	week-day					
	7-7	8-7	9–7	10-7	11-7	12-7	13-7
0 mag	30.9± 1.5	31.8± 1.5	33.2± 1.7	33.6± 1.8	34.7± 1.5	35.3± 1.6	36.5± 1.9
300 ppm	27.8± 1.2**	27.9± 1.3**	28.7± 1.4**	28.8± 1.4**	29.3± 1.4**	30.1± 1.3**	30.7± 1.4**
440 ppm	26.8± 1.3**	26.9± 1.3**	27.5± 1.4**	27.0± 1.4**	27.7± 1.2**	28.2± 1.3**	29.1± 1.8**
670 ppm	25.7± 0.9**	25.7± 1.0**	26.2± 1.2**	26.1± 1.0**	26.6± 1.1**	26.8± 1.0**	27.5± 1.1**
1000 mag	24.7± 1.0**	24.2± 0.6**	24.9± 0.7**	24.8± 0.8**	25.5± 0.7**	26.2± 1.1**	26.8± 1.0**
1500 ppm	24.0± 1.2**	23.4± 1.0**	23.6± 0.7**	-	-	-	-
Significant difference ;	*:P≦ 0.05	**:P ≦ 0.01		Test of Dunnett			
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APPENDIX B 2-4

BODY WEIGHT CHANGES : SUMMARY, MOSUE: FEMALE

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 UNIT : g REPORT TYPE : A1 13 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

-oup Name	Administration	week-day					
	0-0	1-7	2-7	3–7	4-7	5-7	6–7
mag 0	18.7± 0.8	20.4± 0.5	21.2± 0.7	22.2± 0.8	22.8± 1.0	24.2± 0.7	23.9± 0.9
300 maa	18.5± 1.1	19.9± 1.0	20.1± 1.2*	21.0± 0.9**	21.7 ± 1.3	22.7± 1.2**	22.9± 1.0*
440 ppm	18.6± 0.9	20.0± 1.1	20.4± 1.1	20.7± 1.0**	21.6± 1.0*	22.0± 0.8**	22.9± 1.1*
670 ppm	18.2± 0.6	19.0± 0.4**	20.1± 0.6*	20.5± 0.7**	21.2± 0.6**	21.4± 0.7**	22.1± 0.7**
1000 mag	18.4± 0.9	18.8± 0.4**	19.2± 0.6**	19.9± 0.6**	20.5± 0.8**	20.6± 0.6**	21.4± 0.7**
1500 ppm	18.7± 1.1	18.8± 0.8**	18.3± 0.7**	19.3± 0.7**	19.9± 0.8**	19.8± 0.8**	20.5± 0.8**
Significant differen	nce; *:P≦0.05	** : P ≤ 0.01		Test of Dunnett			

BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

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STUDY NO. : 0192 ANIMAL : MOUSE BDF1 UNIT : g REPORT TYPE : A1 13 SEX : FEMALE

PAGE: 4

> Name	Administration	week-day					· · · · · · · · · · · · · · · · · · ·
	7-7	8-7	9-7	10-7	11-7	12-7	13-7
maq 0	24.5± 0.9	24.6± 0.9	25.3 ± 1.4	25.4± 1.9	25.4± 0.8	26.2± 1.4	26.4± 1.6
300 ppm	23.3± 0.9*	23.8± 1.4	24.1± 1.1	23.9± 0.6	24.4± 0.9*	24.2± 1.0**	24.7± 1.4**
440 ppm	22.7± 0.9**	22.7± 0.7	23.1± 1.2**	23.0± 1.1*	23.8± 0.7**	24.1± 1.0**	24.3± 0.9**
670 ppm	21.9± 0.8**	22.2± 0.5**	22.6± 0.7**	22.5± 0.8**	23.1± 0.9**	23.2± 0.9**	23.5± 0.8**
1000 mag	21.2± 0.8**	21.2± 0.5**	21.4± 0.5**	21.1± 0.7**	21.2± 0.6**	22.3± 0.8**	22.9± 0.7**
1500 ppm	20.8± 0.9**	20.6± 1.1**	20.9± 0.9**	20.3± 0.5 ?	-	-	-
	*:P≤ 0.05	** : P ≦ 0.01	• 	Test of Dunnett			

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APPENDIX B 3-1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE (THIRTEEN-WEEK STUDY) STUDY NO. : 0191 ANIMAL : RAT F344 UNIT : g REPORT TYPE : A1 13 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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p Name	Administration	week-day(effective)					
	1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
0 mada	15.8± 0.9	17.4± 1.2	17.2± 1.2	17.5± 1.2	17.7 ± 1.2	17.2± 1.4	16.7± 1.5
190 ppm	15.7± 1.0	16.5± 1.9	16.3± 1.6	17.4± 1.9	18.0± 1.8	18.4± 1.4	17.6± 1.2
380 maa	15.3± 1.4	16.5± 1.5	16.5± 1.5	17.1± 1.7	17.4± 1.9	17.1± 2.0	16.1± 1.6
750 mag	15.2± 0.9	16.0± 1.3	15.5± 1.1	16.3± 1.7	15.2± 1.2*	15.0± 1.3*	14.3± 1.3**
1500 ppm	14.1± 0.8**	14.6± 0.5**	14.9± 0.8**	14.9± 1.2**	14.3± 1.5**	13.7± 1.6**	13.3± 1.7**
3000 ppm	12.8± 1.2**	11.4± 2.6**	12.2± 2.4**	11.6± 1.9**	11.2± 2.7**	11.7± 2.4**	10.8± 1.8**
Significant differe	ence; *:P≦0.05	**:P≦ 0.01		Test of Dunnett			
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STUDY NO. : 0191 ANIMAL : RAT F344 UNIT : g REPORT TYPE : A1 13 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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oup Name	Administration	week-day(effective)					
	8–7(7)	9–7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)	
0 pom	16.8± 1.7	17.7± 1.7	16.8± 1.7	16.9± 1.5	16.5± 1.3	16.7± 1.2	
190 ppm	16.8± 1.2	17.0± 1.6	16.6± 1.5	17.4± 1.4	16.6± 1.4	16.4± 1.2	
380 ppm	15.9± 2.0	16.1± 2.3	15.7 ± 1.8	16.9± 1.8	16.1± 1.2	16.0± 1.0	
750 ppm	13.8± 1.2**	13.3± 1.0**	13.2± 1.4**	14.6± 1.3*	14.3± 1.2	14.6± 1.0*	
1500 ppm	12.4± 1.9**	11.4± 1.6**	10.4± 1.4**	12.4± 2.0**	12.6± 2.2**	13.1± 1.7**	
3000 ppm	10.3± 1.7**	10.7± 1.6**	9.7± 2.3**	10.2± 2.0**	9.7± 3.5**	10.7± 3.1**	
Significant differe	ence; *:P≦0.05	** : P ≦ 0.01		Test of Dunnett			
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APPENDIX B 3-2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE (THIRTEEN-WEEK STUDY) STUDY NO. : 0191 ANIMAL : RAT F344 UNIT : g REPORT TYPE : A1 13 SEX : FEMALE

380 ppm

12.3± 0.8

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

12.5± 1.0

12.4± 0.9

SEX : FEMALE								PAGE : 3
Group Name	Administration 1-7(7)	week-day(effectiue) 2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)	
maq 0	12.4± 0.7	13.1± 0.5	12.7± 1.0	13.0± 0.9	14.4± 1.3	12.8± 0.9	11.7± 1.0	
190 mag	12.4± 0.4	12.0± 0.6	12.2± 1.2	12.6± 1.0	13.1± 1.5	12.9± 1.3	11.6± 0.9	

12.9± 0.6

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12.8± 1.0*

12.3± 0.7

 11.5 ± 0.7

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Significant difference ;	*:P≦ 0.05	** : P ≦ 0.01		Test of Dunnett				
3000 ppm	9.9± 0.7**	7.9± 1.3**	8.6± 1.0**	7.3± 1.1**	7.4± 1.5**	7.9± 1.7**	8.2± 2.5**	
1500 ppm	11.0± 0.7**	11.0± 1.3**	11.7± 1.2	11.4± 1.3**	10.7± 1.3**	10.3± 1.1**	9.7± 0.9**	
750 ppm	12.0± 0.7	12.4± 1.0	11.9± 1.2	12.4 ± 1.3	12.4± 1.3**	11.9± 1.0	10.7± 0.8	

STUDY NO.: 0191 ANIMAL: RAT F344 UNIT: g REPORT TYPE: A1 13 SEX: FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

oup Name	Administration	week-day(effective)					······
	8-7(7)	9–7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)	
mqq 0	11.0± 0.9	12.1± 1.2	11.3± 0.9	11.3± 0.9	11.6± 1.0	11.7± 0.9	
190 mag	11.3± 0.9	12.2± 1.0	11.0± 0.8	11.3± 1.1	11.7± 1.3	12.1± 0.8	
380 ppm	11.3± 0.7	11.3± 1.2	11.1± 0.8	11.6± 1.0	11.4± 0.9	11.2± 1.0	
750 ppm	10.6± 0.8	10.6± 1.2*	10.3± 1.3	10.7± 1.0	10.4± 1.1	11.0± 0.9	
1500 ppm	9.3± 1.3**	8.9± 1.0**	8.3± 1.1**	9.6± 1.3**	9.0± 1.5**	8.8± 1.0**	
3000 ppm	7.2± 1.1**	7.2± 1.0**	6.5± 1.2**	7.1± 1.0**	7.2± 0.9**	7.6± 1.0**	
Significant differer	nce; *:P≦0.05 >	** : P ≦ 0.01		Test of Dunnett			

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BAIS 2

APPENDIX B 3-3

FOOD CONSUMPTION CHANGES : SUMMARY, MOSUE : MALE (THIRTEEN-WEEK STUDY) STUDY NO. : 0192 ANIMAL : MOUSE BDF1 UNIT : g REPORT TYPE : A1 13 SEX : MALE •

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FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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p Name	Administration	week-day(effective)					
	1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7–7 (7)
maq 0	4.3± 0.2	4.2± 0.2	4.2± 0.2	4.6± 0.3	4.6± 0.2	4.6± 0.3	4.4± 0.3
300 mad	4.1± 0.3	4.0± 0.3	4.0± 0.3	4.3± 0.3	4.3± 0.3*	4.1± 0.3**	4.2± 0.3
440 ppm	4.1± 0.3	3.9± 0.3	4.0± 0.3	4.3± 0.2	4.3± 0.3	4.2± 0.2*	4.2± 0.2
670 ppm	3.8± 0.2*	4.2± 0.4	4.6± 0.3	4.5± 0.3	4.4± 0.3	4.4± 0.4	4.6± 0.4
1000 ppm	3.6± 0.2**	4.3± 0.4	4.6± 0.5	4.6± 0.4	4.6± 0.5	4.4± 0.3	4.3± 0.3
1500 ppm	2.3± 1.6**	5.1± 0.6**	5.1± 0.5**	4.9± 0.4	4.6± 0.8	5.3± 0.7**	4.9± 0.3*
Significant differen	ce; *:P≦0.05	** : P ≦ 0.01		Test of Dunnett			
260)							

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 UNIT : g REPORT TYPE : A1 13 SEX : MALE *ر ب*

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PAGE : 2

up Name		week-day(effective)		·····			
	8-7(7)	9–7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)	
mag 0	4.6± 0.3	4.9± 0.3	4.7± 0.3	4.8± 0.3	4.8± 0.3	4.8± 0.4	
300 ppm	4.3± 0.4	4.3± 0.3**	4.4± 0.3	4.3± 0.3**	4.5± 0.2	4.4± 0.3	
440 ppm	4.4± 0.3	4.3± 0.3**	4.4± 0.3	4.5± 0.2	4.6± 0.4	4.7± 0.5	
670 ppm	4.6± 0.4	4.6± 0.4	4.7± 0.3	4.7± 0.5	4.6± 0.4	4.5± 0.5	
1000 ppm	4.5± 0.3	4.7± 0.4	4.6± 0.3	4.5± 0.5	4.7± 0.5	4.6± 0.3	
1500 ppm	5.1± 0.4*	4.9± 0.4	1.7± 0.5**	-		-	
Significant differen	nce; *:P≦0.05	** : P ≦ 0.01		Test of Dunnett			
260)					 		

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APPENDIX B 3-4

FOOD CONSUMPTION CHANGES : SUMMARY, MOSUE : FEMALE (THIRTEEN-WEEK STUDY) STUDY NO.: 0192 ANIMAL : MOUSE BDF1 UNIT : g REPORT TYPE : A1 13 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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PAGE : 3

up Name	Administration	week-day(effective)					
	1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
mag 0	3.6± 0.3	3.6± 0.3	3.9± 0.4	4.1± 0.4	4.4± 0.4	4.2± 0.5	4.4± 0.5
300 ppm	3.5± 0.2	3.4± 0.4	3.8± 0.3	4.1± 0.4	4.2± 0.3	4.1± 0.3	4.3± 0.4
440 ppm	3.4± 0.3	3.5± 0.2	3.7± 0.3	4.0± 0.2	4.0± 0.3	4.0± 0.4	4.2± 0.5
670 ppm	3.1± 0.3**	3.7± 0.2	4.2± 0.5	4.1± 0.4	4.0± 0.3	4.2± 0.3	4.3± 0.3
1000 ppm	3.1± 0.2**	3.7± 0.2	4.2± 0.4	4.3± 0.3	4.3± 0.3	4.3± 0.5	4.2± 0.3
1500 ppm	3.0土 0.2**	3.6± 0.6	4.5± 0.3**	4.4± 0.5	4.4± 0.4	4.4± 0.4	4.3± 0.3
Significant differen	nce; *:P≦0.05	** : P ≦ 0.01		Test of Dunnett			
260)							

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 UNIT : g REPORT TYPE : A1 13 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

Group Name	Administration	week-day(effective)_				······································	
	8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)	
0 mqq	4.5± 0.5	4.6± 0.5	4.7± 0.4	4.5± 0.5	4.7± 0.5	4.7± 0.4	
300 ppm	4.6± 0.5	4.5± 0.4	4.7± 0.4	4.7± 0.5	4.7± 0.5	4.7± 0.6	
440 ppm	4.3± 0.4	4.3± 0.4	4.5± 0.5	4.6± 0.5	4.4± 0.4	4.3± 0.5	
670 ppm	4.6± 0.3	4.6± 0.3	4.8± 0.4	4.8± 0.4	4.7± 0.4	4.5± 0.2	
1000 ppm	4.4± 0.3	4.3± 0.3	4.4± 0.2	3.9± 1.2	4.4± 0.3	4.3± 0.5	

 $4.2\pm$ 0.8 $4.3\pm$ 1.0 $3.1\pm$ 1.3* $1.1\pm$ 1.6 ? -

Significant difference ; $*: P \leq 0.05$ $**: P \leq 0.01$

Test of Dunnett

? : Significant test is not applied, because No. of data in this group is less than 3.

(HAN260)

1500 ppm

BAIS 2

PAGE: 4

APPENDIX B 4-1

HEMATOLOGY : SUMMARY, RAT : MALE

STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE

HEMATOLOGY(1) (SUMMARY) SURVIVAL ANIMALS (14)

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PAGE: 1 Group Name NO. of RED BLOOD CELL HEMOGLOBIN HEMATOCRIT MCV MCH MCHC PLATELET Animals 1 06/µl g / dl % 1 0³ / με fℓ Рg g / dl 0 ppm 10 9.67± 0.24 $16.7 \pm$ 0.4 47.3 ± 1.4 48.9± 1.1 $17.2 \pm$ 0.2 35.2± 0.9 $765\pm$ 65 190 ppm 10 9.63± 0.21 $16.7 \pm$ 0.3 46.8± 1.0 $48.5\pm$ 0.6 $17.3 \pm$ 0.3 $35.6\pm$ 0.6 $781\pm$ 54 380 ppm 9 9.73± 0.20 $16.7 \pm$ 0.3 47.5± 1.2 48.8± 0.7 $17.2 \pm$ 0.2 $35.2 \pm$ 0.8 $814 \pm$ 59 10 9.47± 0.24 39 750 ppm $16.6 \pm$ 0.3 46.7± 0.7 49.3± 0.8 $17.5 \pm$ 0.3 35.5± 0.5 800± 1500 ppm 9 8.89± 0.30** 75** $15.6 \pm$ 0.6** $44.2 \pm$ 1.8** 49.8± 0.7 $17.6 \pm$ 0.6 35.3± 1.2 909± 3000 ppm 8 8.25± 0.27** $14.6 \pm$ 0.6** 43.1± 1.8** $52.3 \pm$ 0.8** $17.7\pm$ 33.9± 0.6** 968± 130** 0.4* Significant difference ; $*: P \leq 0.05$ ** : P ≦ 0.01 Test of Dunnett

(HCL070)

BAIS 2

STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE

HEMATOLOGY(2) (SUMMARY)

SURVIVAL ANIMALS (14)

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PAGE: 1

oup Name	NO. of Animals	WBC 1 0 ³ /1	με	Different N-BAND		(%) N-SEG		EOSINC)	BASO		MONO		LYMPH	0	OTHER		
0 mada	10	4.61±	1.86	1±	1	31±	6	1±	1	0±	0	5±	2	63±	7	0±	0	
190 ppm	10	4.93±	1.25	0±	1	29±	6	2±	1	0±	0	4±	1	$65\pm$	6	0±	0	
380 ppm	9	$5.26\pm$	1.04	0±	0	33±	8	$2\pm$	1	0±	0	4±	1	61±	9	٥±	0	
750 ppm	10	5.96±	2.16	1±	1	30±	8	1±	1	0±	0	$5\pm$	1	64±	8	0±	0	
1500 ppm	9	4.54±	2.04	1±	1	33±	11	1±	1	0±	0	4±	1	61±	12	0±	0	
3000 ppm	8	3.07±	0.93	0±	0	30±	6	1±	1	0±	0	4±	1	65±	6	0±	0	
Significant	t difference ;	*:P≦(0.05	**:P≦	0.01				Test of	Dunnett								
CL71A)																		В

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APPENDIX B 4-2

HEMATOLOGY : SUMMARY, RAT : FEMALE

STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

HEMATOLOGY(1) (SUMMARY) SURVIVAL ANIMALS (14)

up Name	NO. of Animals	RED B 1 O ⁶ /	LOOD CELL µl	HEMOGL g∕dl	OBIN	HEMATC %	OCRIT	MCV fℓ		MCH Pg		MCHC g⁄dl		PLATEL 1 03/4	
0 ppm	10	8.98±	0.35	16.6±	0.5	47.0±	1.8	52.3±	0.5	18.5±	0.2	$35.3 \pm$	0.5	781±	175
190 ppm	10	8.86±	0.23	16.4±	0.4	45.9±	1.2	51.9±	0.4	18.5±	0.4	35.6±	0.6	816±	48
380 ppm	10	8.93±	0.20	16.6±	0.3	46.8±	1.2	52.4±	0.6	18.6±	0.3	35.5±	0.8	803±	64
750 ppm	10	8.97±	0.29	16.4±	0.6	46.2±	1.3	51.5±	0.7	18.3±	0.3	35.4±	0.5	861±	89
1500 ppm	10	8.73±	0.28	15.7±	0.5**	44.4±	1.4**	50.8±	0.5**	17.9±	0.5**	35.3±	1.0	846±	99
3000 ppm	10	8.04±	0.35**	$14.5 \pm$	0.6**	$43.1\pm$	1.4**	$53.7 \pm$	1.2	18.0±	0.4*	$33.5\pm$	0.6**	890±	150

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PAGE: 2

STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

HEMATOLOGY(2) (SUMMARY) SURVIVAL ANIMALS (14)

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PAGE: 2

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oup Name	NO. of Animals	WBC 1 0 ³ /	μ£	Different N-BANI		(%) N-SEG		EOSING)	BASO		MONO		LYMPHO)	OTHER		
0 mag	10	3.41±	2.05	1±	1	30±	8	$2\pm$	1	0±	0	4±	1	64±	8	0±	0	
190 ppm	10	3,50±	0.86	1±	1	25±	4	$2\pm$	1	0±	0	5±	1	68±	4	0±	0	
380 mag	10	2.98±	1.25	1±	1	27±	6	2±	1	0±	0	4±	· 1	66±	7	0±	0	
750 ppm	10	3.28±	1.37	1±	1	26±	6	$2\pm$	1	0±	0	4±	1	68±	6	0±	0	
1500 ppm	10	3.39±	0.98	1±	I	26±	4	2±	1	0土	0	$4\pm$	2	68±	4	0土	0	
3000 ppm	10	3.61±	1.31	$1\pm$	1	23±	5	1±	1*	0±	0	$5\pm$	1	71±	6	0±	0	
Significant	difference;	*:P≦	0.05	** : P ≦	0.01				Test of	Dunnett								
CL71A)																		Ē

APPENDIX B 4-3

HEMATOLOGY : SUMMARY, MOSUE : MALE

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

HEMATOLOGY(2) (SUMMARY) SURVIVAL ANIMALS (14)

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Group Name NO. of WBC Differential WBC (%) Animals 1 0³/µl N-BAND N-SEG EOSINO BASO MONO LYMPHO OTHER 0 ppm 10 1.59± 0.89 $2\pm$ $19\pm$ $1\pm$ 1 4 1 0± 0 $4\pm$ 1 $75\pm$ 4 0± 0 300 ppm 9 0.88± 0.75 $2\pm$ $20\pm$ 8 0± 1 0± 0 5± 1 1 $74\pm$ 9 $0\pm$ 0 440 ppm 10 1.20 ± 0.71 $1\pm$ 1 $19\pm$ 6 1土 1 0± 0 $4\pm$ 2 $75\pm$ 5 0± 0 670 ppm 10 1.29± 0.88 $1\pm$ $16\pm$ 6 0 5 1 0± 1 0± 4土 2 $79\pm$ 0± 0 1000 ppm 8 0.86± 0.41 $1\pm$ $17\pm$ 10 $1\pm$ 0± 0 $4\pm$ 2 $77\pm$ 0± 1 1 9 1 1500 ppm 0 -_ --------_ ----Significant difference ; $*: P \leq 0.05$ ** : P ≦ 0.01 Test of Dunnett

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BAIS 2

PAGE: 1

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

HEMATOLOGY(1) (SUMMARY) SURVIVAL ANIMALS (14)

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oup Name	NO. of Animals	RED BI 1 O ⁶ /1	LOOD CELL	HEMOGL g∕dl		НЕМАТС %	CRIT	MCV fℓ		MCH Pg		MCHC g / dl		PLATEL 1 0 ³ /4	
0 mada	10	10.71±	0.22	16.0±	0.3	47.5±	1.2	44.4±	0.7	14.9±	0.2	33.7±	0.6	$1451\pm$	100
300 ppm	9	10.54±	0.34	15.9±	0.3	46.6±	0.9	44.3±	1.2	15.1±	0.3	34.1±	0.5	1456土	82
440 ppm	10	10.41±	0.22	15.7±	0.3	46.6±	0.8	44.8±	0.7	15.1±	0.2	33.8±	0.3	1514±	103
670 ppm	10	10.39±	0,33*	15.8±	0.4	47.0±	1.7	45.3±	0.5*	15.3±	0.2*	33.7±	0.5	1571±	140
1000 ppm	8	10.35±	0.20*	15.9±	0.4	47.3±	0.7	45.7±	0.4**	15.3±	0.2**	33.5±	0.5	$1723\pm$	110**
1500 ppm	0	-		-				-		_		-		-	

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(HCL070)

BAIS 2

PAGE: 1

APPENDIX B 4-4

HEMATOLOGY : SUMMARY, MOSUE : FEMALE

STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

oup Name	NO. of Animals	TOTAL F g/dl	ROTEIN	ALBUMIN g⁄dê		A/G RAT	.10	T-BILI ng∕dl		GLUCOSE mg⁄dl		T-CHOLES mg/dl	STEROL	TRIGLYCI mg⁄dl	ERIDE
0 mada	10	6.9±	0.2	3.9±	0.1	1.3±	0.1	0.25±	0.05	203±	21	67±	7	95±	44
190 ppm	10	6.9±	0.2	3.8±	0.1	1.3±	0.1	0.26±	0.06	202±	17	65±	7	111±	35
380 ppm	9	7.1±	0,3	4.0±	0.2	1.3±	0.0	0.27±	0.06	$204\pm$	18	72±	10	$120\pm$	35
750 ppm	10	7.1±	0.1	4.0±	0.1	1.3±	0.1	0.28±	0.08	187±	12	72±	11	100±	10
1500 ppm	9	7.1±	0.3	4.2±	0.3*	1.4±	0.1**	0.23±	0.03	172±	22**	99±	15**	73±	13
3000 maa	8	7.1±	0.3	4.1±	0.1**	1.4±	0.1*	0.23±	0.03	$142\pm$	17**	108±	18**	38±	. 9**
Significant	difference;	*:P≦().05	**:P≦0.0	91		····	Test of Du	nnett						·
CL074)													· · · ·		· · ·

PAGE: 1

STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)

SURVIVAL	ANIMALS	(14)
DOWATAND	MALIARO	(14)

: MALE							•								PAGE :
up Name	NO. of Animals	PHOSPHO mg/dl	LIPID	GOT IU/¢		GPT IU∕ℓ		LDH IU/4	?	ALP IU/l		G-GTP IU∕ℓ		CPK IU/l	
0 ppm	10	$122\pm$	9	74±	15	26±	5	203±	114	$332\pm$	34	1±	1	92±	21
190 ppm	10	118±	10	72±	12	25±	5	171±	47	326±	38	1±	1	92±	12
380 ppm	9	131±	14	67±	5	22±	3	165±	13	$335\pm$	50	1±	1	81±	5
750 ppm	10	131±	18	67±	12	22±	3	167土	39	329±	31	1±	0	76±	11
1500 ppm	9	· 163±	22**	55±	6**	18±	2**	167±	27	277±	33*	1±	1	70±	7*
3000 ppm	8	166±	27**	66±	14	25±	14	189±	40	309±	46	3±	5	69±	16*

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STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	UREA NI mg∕dl		CREATIN mg/dl	INE	SODIUM mEq∕ℓ	<u></u>	POTASSI mEq⁄		CHLORIDE mEq / l		CALCIU mg/dl		INORGAN mg/dl	IC PHOSPHORU
0 maga	10	17.4±	1.4	0.6±	0.1	$143\pm$	1	3.3±	0.2	106±	1	10.4±	0.2	5.4±	0.9
190 ppm	10	17.2±	1.8	0.5±	0.0	$143\pm$	1	3.2±	0.2	106±	1	10.3±	0.2	4.9±	0.8
380 ppm	9	18.3±	1.9	0.5±	0.1	$143\pm$	2	3.1±	0.2	105±	1	10.4±	0.1	4.7±	0.8
750 ppm	10	18.5±	1.3	0.5±	0.0*	$143\pm$	1	3.5±	0.3	106±	0	10.4±	0.2	4.8±	0.9
1500 ppm	9	17.0±	1.7	0.5±	0.1*	$144\pm$	2	$3.4\pm$	0.2	108±	2	10.5±	0.2	4.7±	0.8
3000 ppm	8	16.9±	2.6	0.5±	0.0**	$145\pm$	2*	$3.7\pm$	0.3**	108±	2**	10.4±	0.1	5.8±	0.8

Significant difference ; $*: P \leq 0.05$ ** ; P ≦ 0.01 Test of Dunnett

(HCL074)

BAIS 2

PAGE : 3

APPENDIX B 5-1

BIOCHEMISTRY : SUMMARY, RAT : MALE

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

HEMATOLOGY(2) (SUMMARY) SURVIVAL ANIMALS (14)

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PAGE: 2

oup Name	NO. of Animals	WBC 1 0 ³ /	μ£	Different N-BAND		(%) N-SEG		EOSING)	BASO		MONO		LYMPH	0	OTHER		
mqq 0	8	0.83±	0.45	2±	1	$21\pm$	10	0±	1	0±	0	$4\pm$	2	74±	10	0±	0	
300 ppm	10	1.21±	0.94	2±	2	$21\pm$	8	0±	0	0±	0	$4\pm$	2	$74\pm$	9	0±	0	
440 ppm	10	0.69±	0.30	1±	1	22±	12	0±	0	0±	0	$3\pm$	1	74±	12	0±	0	
670 ppm	10	0.94±	0.61	1±	1	18±	7	1±	1	0±	0	4±	1	77±	6	0±	0	
1000 ppm	9	1.17±	0.77	2±	1	17±	5	0±	1	0±	0	4±	1	76±	5	0±	0	
1500 ppm	0	-		-		-				,		-		-		-		
Significant	difference ;	*:Р≦	0.05	**:P≦	0.01				Test of	Dunnett						<u> </u>		
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STUDY NO. : 0192 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

HEMATOLOGY(1) (SUMMARY) SURVIVAL ANIMALS (14)

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Group Name NO. of RED BLOOD CELL HEMOGLOBIN HEMATOCRIT MCV MCH MCHC PLATELET Animals 1 06/µe g / dl % fℓ 1 0³ ⁄ με рg g / dl 0 ppm 8 10.68± 0.36 $16.2 \pm$ 0.5 46.8± 1.3 43.8± 0.5 $15.2 \pm$ 0.1 $34.7 \pm$ 0.4 $1315\pm$ 124 300 ppm 10 10.60± 0.30 $16.2 \pm$ 0.4 47.2± 1.2 44.6± 0.7* $15.3\pm$ 0.3 $34.4\pm$ 0.5 $1357\pm$ 141 440 ppm 10 10.46± 0.14 0.3 $47.3 \pm$ $45.2 \pm$ 0.2 $1349\pm$ 100 $16.1 \pm$ 0.9 0.4** $15.4 \pm$ $34.1 \pm$ 0.5 670 ppm 10 10.31 ± 0.43 $15.9 \pm$ 0.5 $46.7 \pm$ 1.9 45.3± 0.6** $15.5 \pm$ 0.3 $34.1\pm$ 0.7 $1380\pm$ 229 1000 ppm 9 10.32 ± 0.37 $15.9 \pm$ 0.4 46.6± 1.6 $45.2 \pm$ 0.5** $15.4 \pm$ 0.3 $34.0 \pm$ 0.6 $1530\pm$ 122* 1500 ppm 0 ----_ _ _ --------Significant difference ; $*: P \leq 0.05$ ** : P ≦ 0.01 Test of Dunnett

(HCL070)

BAIS 2

PAGE : 2

APPENDIX B 5-2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

up Name	NO. of Animals	TOTAL F g⁄dl		ALBUMIN g⁄dl		A/G RAT	10	T-BILI mg/dl		GLUCOSE		T-CHOLES mg/dl	STEROL	TRIGLYCE mg/dl	ERIDE
0 ppm	10	6.6±	0.2	3.7±	0.1	1.3±	0.1	0.27±	0.10	129±	18	92±	6	$42\pm$	6
190 ppm	10	6.5±	0.2	$3.7\pm$	0.1	1.3±	0.1	0.24±	0.02	$137\pm$	15	87±	6	42±	4
380 ppm	10	6.5±	0.2	3.6±	0.1	1.3±	0.0	0.29±	0.18	$135\pm$	17	89±	10	42±	6
750 ppm	10	6.4±	0.2	3.6±	0.1	1.3±	0.1	0.31±	0.15	$131\pm$	24	$91\pm$	7	41土	5
1500 ppm	10	6.5±	0.2	3.7±	0.2	1.3±	0.1	0.28±	0.06	146±	21	$112\pm$	11**	$45\pm$	6
3000 ppm	10	6.5±	0.3	3.8±	0.1	1.4±	0.1**	0.49±	0.38	118±	13	$117\pm$	10**	42±	14

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STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

up Name	NO. of Animals	PHOSPHO mg/dl	LIPID	GOT IU/	?	GPT IU/4	ę	LDH IU/	e	ALP IU/4		G-GTP IU∕ℓ		CPK IU/e	
mag 0	10	159±	14	123±	160	62±	118	645±	1298	245±	43	2±	1	127±	65
190 ppm	10	$153\pm$	12	75±	14	23±	6	201±	38	243±	28	1±	1	95±	11
380 ppm	10	153±	15	69±	9	21±	6	209±	58	249±	35	1±	1	98±	17
750 ppm	10	158±	14	$121\pm$	153	55±	96	$513\pm$	943	$250\pm$	30	1±	1	110±	62
1500 ppm	10	185±	16**	61±	5*	20±	2	$234\pm$	82	278±	46	3±	1	84±	18
3000 ppm	10	190±	13**	70±	4	22±	2	395±	138*	320±	68**	6±	1**	102±	36

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

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REPORT TYPE : A1 SEX : FEMALE

STUDY NO. : 0191 ANIMAL : RAT F344

PAGE: 6

	18.5± 18.2± 18.0±	3.5 1.4 1.4	0.6± 0.5± 0.6±	0.1 0.0 0.1	143± 143±	2	3.1± 3.3±	0.1	110± 110±	2	10.0±	0.3 0.3	4.8± 4.7±	1.7
I						1	3.3±	0.2	110±	1	10.0±	0.3	A 7+	1 4
	18.0±	1.4	0.6±	0.1	140.1								4.11	1.4
					143±	2	3.1±	0.2	110± ·	1	10.0±	0.2	5.0±	0.9
	20.0±	3.7	0.5±	0.0	$143\pm$	2	3.3±	0.2	109±	1	9.9±	0.2	5.0±	1.6
	19.2±	2.8	0.5±	0.1	$144\pm$	2	$3.4\pm$	0.3*	110±	1	9.9±	0.3	5.0±	1.1
	19.1±	3.5	0.4±	0.0**	$146\pm$	2**	3.7±	0.4**	109±	2	9.9±	0.3	6.1±	1.4
nce; *	: P ≦ 0.	.05 *	**:P≦0.0)1			Test of Dur	nett						
1	IC9; *	19.1±	19.1± 3.5	19.1± 3.5 0.4±	19.1± 3.5 0.4± 0.0**	19.1± 3.5 0.4± 0.0** 146±	19.1± 3.5 0.4± 0.0** 146± 2**	19.1± 3.5 0.4± 0.0** 146± 2** 3.7±	19.1± 3.5 0.4± 0.0** 146± 2** 3.7± 0.4**	19.1± 3.5 0.4± 0.0** 146± 2** 3.7± 0.4** 109±	19.1± 3.5 0.4± 0.0** 146± 2** 3.7± 0.4** 109± 2	19.1± 3.5 0.4± 0.0** 146± 2** 3.7± 0.4** 109± 2 9.9±	19.1± 3.5 0.4± 0.0** 146± 2** 3.7± 0.4** 109± 2 9.9± 0.3	$19.1 \pm$ 3.5 $0.4 \pm$ $0.0 * *$ $146 \pm$ $2 * *$ $3.7 \pm$ $0.4 * *$ $109 \pm$ 2 $9.9 \pm$ 0.3 $6.1 \pm$

APPENDIX B 5-3

BIOCHEMISTRY : SUMMARY, MOSUE : MALE

STUDY NO. : 0192

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BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

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ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

oup Name	NO. of Animals		TAL PROTEIN		UMIN ⁄dê	۸/G	RATIO		BILIRUBIN /dl	GLU ng/	COSE 'dl	T-CI mg⁄	IOLESTEROL 'al	TRIC mg/	GLYCERIDE 'al
0 ppm	10	5.4±	0.2	2.9±	0.1	1.1±	0.1	0.40±	0.15	191±	23	86±	7	64±	13
300 ppm	9	5.4±	0.2	2.9±	0.1	1.2±	0.1	0.32±	0.12	$143\pm$	14**	80±	9	$45\pm$	12**
440 ppm	10	5.4±	0.2	2.9±	0.1	$1.2\pm$	0.1	0.38±	0.10	$147\pm$	19**	74±	6	48±	11**
670 ppm	10	5.5±	0.3	3.1±	0.2**	1.3±	0.1**	0.37±	0.11	143±	17**	75±	11	$45\pm$	10**
1000 ppm	8	5.5±	0.2	$3.1\pm$	0.1**	1.3±	0.1**	0.38±	0.07	135±	34**	78±	14	48±	8*
1500 ppm	0	-		-		-		_		-				-	

? : Significant test is not applied, because No. of data in this group is less than 3.

(HCL074)

BAIS 2

PAGE: 1

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STUDY NO. : 0192

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

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ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

up Name	NO. of Animals	GOT I U	J / E	GPT I U	/ ę	LDH I (J/l	ALP I U	J∕€		J⁄ł		EA NITROGEN ⁄dl	SODI mEq	
0 ppm	10	49±	6	14±	4	318±	121	199±	13	68±	28	24.1±	3.4	154±	2
300 ppm	9	48±	9	14±	4	244±	38	206±	16	$44\pm$	10*	28.5±	4.1	154±	1
440 ppm	10	$52\pm$	11	14±	4	300±	76	208±	10	$55\pm$	17	29.9±	2.4**	153±	2
670 ppm	10	47±	9	13±	4	279±	55	$225\pm$	12**	48±	12	28.1±	4.2	154±	2
1000 ppm	8	$54\pm$	11	17±	8	305±	64	269±	19**	61±	18	29.9±	7.1	$155\pm$	2
1500 ppm	0	-		-		-		_		-		-		-	
Significant	difference;	*:P	≤ 0.05	**:P≦	0.01			Test of	Dunnett				<u> </u>		

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?: Significant test is not applied, because No. of data in this group is less than 3.

(HCL074)

BAIS 2

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

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oup Name	NO. of Animals	POTASSIUM mEq∕ℓ	CHLORIDE mEq∕ℓ	CALCIUM mg⁄dl	INORGANIC PHOSPHORUS mg/dl	
0 ppm	10	4.7± 0.5	123 ± 1	8.9± 0.2	8.1± 0.9	
300 ppm	9	4.5± 0.5	122± 2	8.7± 0.3	7.3± 0.8	
440 ppm	10	4.7± 0.5	122± 3	8.7± 0.3	7.3± 0.6	
670 ppm	10	4.8± 0.6	122± 3	8.6± 0.3	7.5± 1.2	
1000 ppm	8	4.9± 0.3	122± 3	8.7± 0.3	8.7± 1.2	
1500 ppm	0	-	-	-	-	
Significant	difference :	*:P≦0.05	** : P ≦ 0.01		Test of Dunnett	

?: Significant test is not applied, because No. of data in this group is less than 3.

(HCL074)

BAIS 2

PAGE: 3

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APPENDIX B 5-4

BIOCHEMISTRY : SUMMARY, MOSUE : FEMALE

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

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p Name	NO. of Animals		AL PROTEIN		UMIN ⁄dl	A/G	RATIO		BILIRUBIN ⁄dl		COSE ⁄dl	T-Cl ng/	IOLESTEROL 'dl	TRIC mg/	GLYCERIDE 'de
0 ppm	8	5.3±	0.3	3.1±	0.2	1.4±	0.1	0.24±	0.06	140±	43	64±	12	48±	16
300 ppm	10	5.5±	0.2	3.2±	0.1	1.4±	0.1	0.35±	0.09	$135\pm$	15	77±	15*	$44\pm$	8
440 ppm	10	5.5±	0.2	$3.2\pm$	0.2	1.4±	0.1	0.36±	0.12	$151\pm$	25	82±	10**	$46\pm$	9
670 ppm	9	5.5±	0.2	$3.2\pm$	0.1	1.4±	0.1	0.34±	0.08	$152\pm$	29	82±	9**	45±	9
1000 ppm	9	5.4±	0.2	3.2±	0.1	1.5±	0.1*	0.35±	0.14	$151\pm$	29	82±	5**	$45\pm$	9
1500 ppm	0	-		-		-		-		-		-		-	

?: Significant test is not applied, because No. of data in this group is less than 3.

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BAIS 2

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STUDY NO. : 0192

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BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

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ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

p Name	NO. of Animals	GOT I U	J / Q	GPT I U	/ e	LDI I I	[] / l	ALP I L	1/0	CPX I T	J/l		A NITROGEN	SODI m ^E q	
0 ppm	8	$62\pm$	11	14±	3	278±	69	$341\pm$	29	58±	26	20.1±	3.8	$152\pm$	2
300 ppm	10	80±	49	19±	9	414±	310	333±	40	159±	233	23.2±	2.7	$152\pm$	2
440 ppm	10	72±	24	16±	3	364±	151	326±	64	101±	63	21.8±	3.7	$153\pm$	2
670 ppm	9	61±	17	$15\pm$	6	287±	109	$359\pm$	59	80±	65	22.3±	3.0	153±	2
1000 mam	9	53±	6	14±	4	$266\pm$	55	370±	44	75±	28	21.9±	1.5	$153\pm$	2
1500 ppm	0	-		_		-		-		-		-		-	

?: Significant test is not applied, because No. of data in this group is less than 3.

(HCL074)

BAIS 2

STUDY NO. : 0192

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BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

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ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

PAGE: 6

p Name	NO. of Animals		CASSIUM Eq∕ℓ	CHLO mEq			CIUM ⁄dջ	INORGANIC mg/dl	; PHOSPHORUS
mag 0	8	4.6±	0.6	121±	3	8.8±	0.3	7.0± 0.3	
300 ppm	10	4.4±	0.2	$120\pm$	4	8.7±	0.4	6.8± 1.0	
440 ppm	10	4.5±	0.2	123±	2	9.0±	0.5	6.9± 0.9	
670 ppm	9	4.7±	0.5	$124\pm$	2	8.9±	0.4	7.0± 1.1	
1000 ppm	9	4.5±	0.3	$123\pm$	2	8.7±	0.4	6.9± 1.3	
1500 ppm	0	-		-		-		-	

?: Significant test is not applied, because No. of data in this group is less than 3.

(HCL074)

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APPENDIX B 6-1

URINALYSIS : SUMMARY, RAT : MALE

STUDY NO. : 0191 ANIMAL : RAT F344 SAMPLING DATE : 013-6 SEX : MALE REPORT TYPE : A1

URINALYSIS

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NO. of	рH							Protei	n			GLu	cose			Ket	nne bo	ΗV		Bi	irubi	1	
Animals	5.0	6,0	6.5	7.0	7.5	8.0	8.5 CHI			2+ 3	3+ 4+ CHI				3+ 4+ CHI				4+ CHI				
10	0	0	0	2	0	8	0	0 1	6	3	0 0	10	0	0 0	0 0	4	6 0	0 0	0	10	0 0	0	
10	0	0	0	0	1																		
10	0	0	1	0	3	6	0	0 0	6	4	0 0	10	0	0 0	0 0	5	50	0 0	0	10	0 0	0	
10	0	0	0	1	1	8	0	0 1	5	4	0 0	10	0	0 0	0 0	4	5 1	0 0	0.	10	0 0	0	
10	0	0	0	2	2	6	0	02	6	2	0 0	10	0	0 0	0 0	6	4 0	0 0	0	10	0 0	0	
9	0	0	0	0	3	6	0	1 2	4	2	0 0	9	0	0 0	0 0	3	51	0 0	0	9	0 0	0	
			0	0	ა 	ь		1 2	4	2	0 0	9	0	· · ·	0 0	3	51	0 0	0	9	0 0	0	
difference	; *:	: P ≦	0.05	5	** :	P ≦	0.01				Tes	t of CH	II SQ	UARE									
	Animals 10 10 10 10 10 9	Animals 5.0 10 0 10 0 10 0 10 0 10 0 10 0 9 0	Animals 5.0 6.0 10 0 0 10 0 0 10 0 0 10 0 0 10 0 0 10 0 0 10 0 0 9 0 0	Animals 5.0 6.0 6.5 10 0 0 0 10 0 0 0 10 0 0 1 10 0 0 1 10 0 0 0 10 0 0 0 10 0 0 0 9 0 0 0	Animals 5.0 6.0 6.5 7.0 10 0 0 0 2 10 0 0 0 0 10 0 0 10 0 10 0 0 1 0 10 0 0 1 0 10 0 0 0 1 10 0 0 0 2 9 0 0 0 0	Animals 5.0 6.0 6.5 7.0 7.5 10 0 0 0 2 0 10 0 0 0 1 10 0 0 1 0 10 0 0 1 1 10 0 0 1 1 10 0 0 1 1 10 0 0 2 2 9 0 0 0 3	Animals 5.0 6.0 6.5 7.0 7.5 8.0 10 0 0 0 2 0 8 10 0 0 0 1 8 10 0 0 1 0 3 6 10 0 0 1 1 8 10 0 0 1 1 8 10 0 0 0 1 1 8 10 0 0 0 2 2 6 9 0 0 0 3 6	Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI 10 0 0 0 2 0 8 0 10 0 0 0 1 8 1 10 0 0 1 0 3 6 0 10 0 0 1 1 8 0 10 0 0 1 1 8 0 10 0 0 1 1 8 0 10 0 0 1 1 8 0 10 0 0 2 2 6 0 9 0 0 0 3 6 0	Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI $-\pm$ 10 0 0 0 2 0 8 0 0 1 10 0 0 0 1 8 1 0 0 10 0 0 1 0 3 6 0 0 0 10 0 0 1 1 8 0 0 1 10 0 0 1 1 8 0 0 1 10 0 0 2 2 6 0 2 2 9 0 0 0 3 6 0 1 2	Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI $-\pm +$ 10 0 0 0 2 0 8 0 0 1 6 10 0 0 0 1 8 1 0 0 7 10 0 0 1 0 3 6 0 0 6 10 0 0 1 1 8 0 1 5 10 0 0 1 1 8 0 0 1 5 10 0 0 2 2 6 0 0 2 6 9 0 0 0 3 6 0 1 2 4	Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI $-\pm +2+3$ 10 0 0 0 2 0 8 0 0 1 6.3 10 0 0 0 1 8 1 0 0.7 3 10 0 0 1 0 3 6 0 0.64 10 0 0 1 1 8 0 0.163 10 0 0 1 1.8 0 0.644 10 0.00 0.22 2.60 0.262 2.9 9 0.00 0.360 0.1242 2.42	Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI $-\pm \pm 2\pm 3\pm 4\pm$ CHI 10 0 0 0 2 0 8 0 0 1 6.3 0 0 10 0 0 0 1 8 1 0 0 7 3 0 0 10 0 0 1 1 8 0 0 6 4 0 0 10 0 0 1 1 8 0 0 1 5 4 0 0 10 0 0 1 1 8 0 0 2 6 0 0 2 6 0 0 2 6 0 0 2 6 0 1 2 4 2 0 0 9 0 0 0 3 6 0 1 2 4 2 0 0	Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI $-\pm \pm 2 + 3 \pm 4 \pm$ CHI $-$ 10 0 0 0 2 0 8 0 0 16 3 0 10 10 0 0 0 1 8 1 0 0 7 3 0 10 10 0 0 1 1 8 1 0 0 7 3 0 10 10 0 0 1 1 8 0 0 15 4 0 10 10 0 0 2 2 6 0 12 4 2 0 9 9 0 0 0 3 6 0 1 2 4 2 0 9	Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI $-\pm +2+3+4+$ CHI $-\pm -\pm -2+3+4+$ CHI $-\pm -2+3+4+$ CHI $-2+3+4+$ CHI $-2+3+4+3+4+$ CHI -2	Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI $-\pm \pm 2\pm 3\pm 4\pm$ CHI $-\pm \pm 2\pm$ 10 0 0 0 1 8 0 0 16 3 0 10 0	Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI $-\pm \pm 2\pm 3\pm 4\pm$ CHI $-\pm \pm 2\pm 3\pm 4\pm$ CHI $-\pm \pm 2\pm 3\pm 4\pm$ CHI 10 0 0 0 1 8 0 0 16 3 0 10 0 0 0 0 10 0 0 0 1 8 1 0 0 7 3 0 10 <	Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI $-\pm \pm 2\pm 3\pm 4\pm$ CHI $-\pm 2\pm 3\pm 4\pm$ CHI $-\pm 2\pm 3\pm 4\pm$ CHI $-\pm 2\pm 3\pm 4\pm$	Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI $-\pm \pm 2 + 3 + 4 +$ CHI $-\pm 2 + 3 + 4 +$ CHI $-$	Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI $-\pm + 2 + 3 + 4 + $ CHI $-\pm$	Animats 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI $-\pm \pm 2 + 3 + 4 +$ CHI 10 0 0 0 1 8 1 0 0 7 3 0 10 0	Animats 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI $-\pm + 2 + 3 + 4 +$ CHI $-\pm + 2 $	Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI $-\pm \pm 2 \pm 3 \pm 4 \pm$ $-\pm \pm 2 \pm 3 \pm 4 \pm$ $-\pm \pm 2 \pm 3 \pm 4 \pm$ $-\pm \pm 2 \pm 3 \pm 4 $	Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI $-\pm + 2+3+4+$ CHI $-\pm + 2+3+$ CHI $-\pm + 2+3+4+$

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PAGE: 1

	Animals	Occult bload $-\pm$ + 2+ 3+ CHI	Urobilinogen ± + 2+ 3+ 4+ CHI	
mqq 0	10	10 0 0 0 0	10 0 0 0 0	
190 ppm	10	10 0 0 0 0	10 0 0 0 0	
380 ppm	10	10 0 0 0 0	10 0 0 0 0	
750 ppm	10	8 2 0 0 0	10 0 0 0 0	
1500 ppm	10	8 2 0 0 0	10 0 0 0 0	
3000 ppm	9	6 1 2 0 0	90000	

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APPENDIX B 6-2

URINALYSIS : SUMMARY, RAT : FEMALE

STUDY NO. : 0191		
ANIMAL : RAT F344		
SAMPLING DATE : 013-6	1	
SEX : FEMALE	REPORT TYPE : A1	

	NO, of Animals	рН <u>_</u> 5.0	6.0	6.5	7.0	7.5	8.0	8.5 CHI	Pro-			+ 3+	- 4+	CHI		zoou +		2+ 3+	· 4+ CHI		:one ± -				CHI		liruł + :		H CI	1	
																				- · · ·			0,								
mqq 0	10	0	0	0	1	4	5	0	1	8	1	0 () ()		10	0	0	0 0	0	10	0	0 0	0 0	0		10	0	0	0		
190 ppm	10	0	0	0	0	1	9	0	0	6	4	0 0	0		10	0	0	0 0	0	10	0	0 0	0	0		10	0	0	0		
380 ppm	10	0	0	0	1	3	6	0	0	6	4	0 0) ()		10	0	0	0 0	0	10	0	0 0	0	0		10	0	0	0		
750 ppm	10	0	0	0	0	2	8	0	0	9	1	0 0) ()		10	0	0	0 0	0	10	0	0 0	0	0		10	0	0	0		
1500 ppm	10	0	0	0	2	3	5	0	0	6	4	0 0) ()		10	0	0	0 0	0	8	2	0 0	0	0		10	0	0	0		
3000 ppm	10	0	0	0	3	3	4	0	0	2	8	0 () ()	**	10	0	0	0 0	0	6	4	0 0	0	0	*	10	0	0	0		

URINALYSIS

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BAIS 2

PAGE: 3

pup Name	NO. of Animals	0ccult blood — ± + 2+ 3+ CHI	Urobilinogen ± + 2+ 3+ 4+ CHI		
0 ppm	10	10 0 0 0 0	10 0 0 0 0		
190 ppm	10	10 0 0 0 0	10 0 0 0 0		
380 ppm	10	10 0 0 0 0	10 0 0 0 0		
750 ppm	10	10 0 0 0 0	10 0 0 0 0		
1500 ppm	10	10 0 0 0 0	10 0 0 0 0		
3000 ppm	10	10 0 0 0 0	10 0 0 0 0		

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APPENDIX B 6-3

URINALYSIS : SUMMARY, MOSUE : MALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 SAMPLING DATE : 013-6 SEX : MALE REPORT TYPE : A1

NO. of pH_ Ketone body_ Occult blood Protein_ Glucose_ Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI - ± + 2+ 3+ 4+ CHI $-\pm$ + 2+ 3+ 4+ CHI $-\pm$ + 2+ 3+ 4+ CHI $-\pm +2+3+$ CHI 0 ppm 10 2 2 2 4 0 0 8 2 0 0 0 0 0 10 0 0 0 0 0 6 3 1 0 0 0 10 0 0 0 0 300 ppm 0 0 1 5 3 1 0 10 0 0 5 5 0 0 10 0 0 0 0 0 3 7 0 0 0 0 10 0 0 0 0 440 ppm 10 0 0 2 2 4 2 0 0 1 5 4 0 0 10 0 0 0 0 0 4 6 0 0 0 0 10 0 0 0 0 670 ppm 10 0 0 0 7 2 1 0 1 5 4 0 0 0 10 0 0 0 0 0 2 6 2 0 0 0 10 0 0 0 0 1000 ppm 8 0 2 3 2 1 0 0 0 0 7 1 0 0 8 0 0 0 0 0 3 4 1 0 0 0 8 0 0 0 0 1500 ppm 0 ? ----? ----? ----? - - - - ? _ ----

Significent difference ; $*: P \leq 0.05$ ** : P ≦ 0.01

Test of CHI SQUARE

? : Significant test is not applied, because No. of data in this group is less than 3.

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Group Name

BAIS 2

PAGE: 1

URINALYSIS

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oup Name	NO. of Animals	Urobilinogen ± + 2+ 3+ 4+ CHI	 		
maa 0	10	10 0 0 0 0			
300 ppm	10	10 0 0 0 0			
440 ppm	10	10 0 0 0 0			
670 ppm	10	10 0 0 0 0			
1000 ppm	8	8 0 0 0 0			
1500 ppm	0	?			

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BAIS 2

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APPENDIX B 6-4

URINALYSIS : SUMMARY, MOSUE : FEMALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0192	
ANIMAL : MOUSE BDF	71
SAMPLING DATE : 013-6	;
SEX : FEMALE	REPORT TYPE : A1

Group Name

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URINALYSIS

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roup Name	NO. of	рĦ						-		Pro	tei	n					Gluo						 Keto	סמו	hod				0~		bloo			
	Animals		6.0	6.5	7.0	7.5	8.0	8.5	CHI				2+ 3	+ 4+	CHI					+ 3	+ 4+	CHI					4+	CHI			+ 2+		CH	I
					<u> </u>																													
0 ppm	10	0	0	3	2	5	0	0		0	1	9	0	0 (10	0	0	0	0 0		2	8	0	0 0	0		10	0	0 (0 0		
300 ppm	10	0	0	1	2	4	3	0		0	1	9	0	0 (10	0	0	0	0 0		4	6	ó	0 0	0		10	0	0 (0 0		
440 ppm	10	0	0	1	3	6	0	0		0	1	7	2	0 0			10	0	0	0	0 - 0		2	7	1	0 0	0		10	0	0 (0 0		
670 ppm	10	0	1	1	5	1	2	0		0	4	5	1	0 (10	0	0	0	0 0		2	8	0	0 0	0		10	0	0 (0 0		
1000 ppm	9	0	0	2	1	4	2	0		0	2	6	1	0 0			9	0	0	0	0 0		5	4	0	0 0	0		9	0	0 (0 0		
1500 ppm	0	-	-	-	-	-	-	-	?	-	-	-	-		?		-	-	-	-		?	-	-	-		· -	?	-	-	- .		?	?
						·																	 											
Significent	difference	; *;	P ≦	i 0.05	5	**	: P ≦	0.01							Tes	t of	CH	I SQ)UAF	Έ														

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? : Significant test is not applied, because No. of data in this group is less than 3.

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PAGE: 3

up Name	NO. of Animals	Urobilinogen ± + 2+ 3+ 4+	СНІ			
0 ppm	10	10 0 0 0 0				
300 ppm	10	10 0 0 0 0				
440 ppm	10	10 0 0 0 0				
670 ppm	10	10 0 0 0 0				
1000 ppm	9	90000				
1500 ppm	0		?			

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APPENDIX B 7-1

GROSS FINDINGS : SUMMARY, RAT: MALE : DEAD AND MORIBUND ANIMALS (THIRTEEN-WEEK STUDY)

STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE		GROSS FINDINGS (SUMMARY) DEAD AND MORIBUND ANIMALS (O-	· 14W)			PAGE: 1
Organ Findin	gs	Group Name NO. of Animals	0 ppm 0 (%)	190 ppm 0 (%)	380 ppm 0 (%)	750 ppm 0 (%)
thymus atroph	nic		- (-)	- (-)	- (-)	- (-)
red			- (-)	- (-)	- (-)	- (-)

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STUDY NO. : 0191 ANIMAL : RAT I REPORT TYPE : A1		GROSS FINDINGS (SUMMARY) DEAD AND MORIBUND ANIMALS (0- 14W)						
SEX : MALE					PAGE : 2			
OrganFi	ndings	Group Name NO. of Animals	1500 ppm 0 (%)	3000 ppm 1 (%)				
thymus at	rophic		- (-)	1 (100)				
ге	d		- (-)	1 (100)				

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APPENDIX B 7-2

GROSS FINDINGS : SUMMARY, RAT : MALE : SACRIFICED ANIMALS

(THIRTEEN-WEEK STUDY)

STUDY NO.	: 0191	GROSS FINDINGS (SUMMARY)
ANIMAL	: RAT F344	SACRIFICED ANIMALS (14W)
REPORT TYPE	: A1	
SEX	: MALE	

0r:gan	Findings	Group Name NO. of Animals 10	0 ppm (%) 1	190 ppm 10 (%)	380 ppm 10 (%)	750 ppm 10 (%)
lung	red	0	(0)	0 (0)	0 (0)	0 (0)
liver	herniation	1	(10)	0 (0)	0 (0)	0 (0)
өуө	turbid	0	(0)	0 (0)	1 (10)	0 (0)
	exophthalmos		(0)	0 (0)	1 (10)	0 (0)

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PAGE: 1

STUDY NO.	: 0191	
ANIMAL	: RAT F344	
REPORT TVPF	: 41	

REPORT TYPE : A1 SEX : MALE

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (14W)

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		······			
Organ	Findings	Group Name NO. of Animals	1500 ppm 10 (%)	3000 ppm 9 (%)	
lung	red		0 (0)	1 (11)	
liver	herniation		0 (0)	0 (0)	
өуө	turbid		0 (0)	0 (0)	
	exophthalmos		0 (0)	0 (0)	

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BAIS 2

PAGE: 2

APPENDIX B 7-3

GROSS FINDINGS : SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS (THIRTEEN-WEEK STUDY)

REPORT TYPE	: 0191 : RAT F344 : A1 : FEMALE	GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (14W)				PAGE : 3
0rgan	Findings	Group Name NO. of Animals	0 ppm 10 (%)	190 ppm 10 (%)	380 ppm 10 (%)	750 ppm 10 (%)
Liver	herniation		1 (10)	1 (10)	0 (0)	1 (10)
(HPT080)						BAIS 2

STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE	GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (14W)	PAGE : 4
Organ Findings	Group Name 1500 ppm 3000 ppm NO. of Animals 10 (%) 10 (%)	
liver herniation	1 (10) 0 (0)	
(1000000)		

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APPENDIX B 7-4

GROSS FINDINGS : SUMMARY, MOSUE : MALE : DEAD AND MORIBUND ANIMALS

(THIRTEEN-WEEK STUDY)

GROSS FINDINGS (SUMMARY) DEAD AND MORIBUND ANIMALS (0- 14W)

ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

STUDY NO. : 0192

SEX	: MALE					PAGE : 1
0rgan	Findings	Group Name NO. of Animals	maq0 (%) 0	300 ppm 0 (%)	440 ppm 0 (%)	670 ppm 0 (%)
lung	red zone		- (-)	- (-)	- (-)	- (-)
spleen	black zone		- (-)	- (-)	- (-)	- (-)
liver	white zone		- ()	- (-)	- (-)	- (-)
kidney	hydronephros i s		- (-)	- (-)	- (-)	- (-)
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# GROSS FINDINGS (SUMMARY) DEAD AND MORIBUND ANIMALS (0- 14W)

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STUDY NO. : 0192 : MOUSE BDF1 ANIMAL REPORT TYPE : A1 SEX : MALE

Group Name 1000 ppm 1500 ppm 2 (%) 10 (%) Organ\_\_\_ Findings NO. of Animals lung 0 ( 0) 1 (10) red zone spleen black zone 1 (50) 0 ( 0) Liver 0 ( 0) white zone 4 (40) 0 ( 0) kidney hydronephrosis 1 (10)

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PAGE: 2

APPENDIX B 7-5

GROSS FINDINGS : SUMMARY, MOSUE : MALE : SACRIFICED ANIMALS (THIRTEEN-WEEK STUDY)

| STUDY NO. : 0192<br>ANIMAL : MOUSE BDF1 | GROSS FINDINGS (SUMMARY)<br>SACRIFICED ANIMALS ( 14W) |
|-----------------------------------------|-------------------------------------------------------|
| REPORT TYPE : A1                        |                                                       |
| SEX : MALE                              |                                                       |

| PAGE | : | 1 |
|------|---|---|
|------|---|---|

| 0rgan  | Findings         | Group Name<br>NO. of Animals | 0 ppm<br>10 (%) | 300 ppm<br>10 (%) | 440 ppm<br>10 (%) | 670 ppm<br>10 (%) |
|--------|------------------|------------------------------|-----------------|-------------------|-------------------|-------------------|
| spleen | black zone       |                              | 0 ( 0)          | 1 (10)            | 3 (30)            | 0 ( 0)            |
| kidney | hydronephros i s |                              | 0 ( 0)          | 1 (10)            | 0 ( 0)            | 0 ( 0)            |
|        |                  |                              |                 |                   |                   |                   |

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| ANIMAL<br>REPORT TYPE | : 0192<br>: MOUSE BDF1<br>: A1<br>: MALE | GROSS FINDINGS (SUMMARY)<br>SACRIFICED ANIMALS ( 14W) |                 |                   | PAGE : 2 |
|-----------------------|------------------------------------------|-------------------------------------------------------|-----------------|-------------------|----------|
| Organ                 | Findings                                 | Group Name<br>NO. of Animals 8                        | 1000 ppm<br>(%) | 1500 ppm<br>0 (%) |          |
| spleen                | black zone                               | 0                                                     | ( 0)            | - ( -)            |          |
| kidney                | hydronephros i s                         | 1                                                     | (13)            | - ( -)            |          |
|                       |                                          |                                                       |                 |                   |          |

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APPENDIX B 7-6

GROSS FINDINGS : SUMMARY, MOSUE : FEMALE : SACRIFICED ANIMALS (THIRTEEN-WEEK STUDY)

| STUDY NO.   | : | 0192       | GROSS FINDINGS (SUMMARY)  |
|-------------|---|------------|---------------------------|
| ANIMAL      | : | MOUSE BDF1 | SACRIFICED ANIMALS ( 14W) |
| REPORT TYPE | : | A1         |                           |
| SEX         | : | FEMALE     |                           |

| Organ  | Findings   | Group Name<br>NO. of Animals 10 | 0 ppm<br>(%) 11 | 300 ppm<br>) (%) | 440 ppm<br>10 (%) 1 | 670 ppm<br>0 (%) |
|--------|------------|---------------------------------|-----------------|------------------|---------------------|------------------|
| spleen | black zone | 0                               | ( 0)            | 0 ( 0)           | 3 (30)              | 0 ( 0)           |
| DUALY  | cyst       | 0                               | ( 0)            | 1 (10)           | 0 ( 0)              | 0 ( 0)           |
|        |            |                                 |                 |                  |                     |                  |

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| ANIMAL<br>REPORT TYPE | : MOUSE BDF1 | INGS (SUMMARY)<br>ANIMALS ( 14W)            |                   | PAGE : 4 |
|-----------------------|--------------|---------------------------------------------|-------------------|----------|
| 0rgan                 | Findings     | Group Name 1000 ppm<br>VO. of Animals 9 (%) | 1500 ppm<br>0 (%) |          |
| spleen                | black zone   | 1 (11)                                      | - ( -)            |          |
| DUary                 | cyst         | 1 (11)                                      | - ( -)            |          |
|                       |              |                                             |                   |          |

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APPENDIX B 8-1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE (THIRTEEN-WEEK STUDY)

STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE UNI

# ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (14)

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| oup Name                                 | NO. of<br>Animals | Body     | Weight | ТНҮМ   | US      | ADRE   | NALS    | TEST       | ES      | HEAR   | Γ       | LUNG   | S       |  |
|------------------------------------------|-------------------|----------|--------|--------|---------|--------|---------|------------|---------|--------|---------|--------|---------|--|
| 0 mana mana mana mana mana mana mana man | 10                | 316±     | 19     | 0.256± | 0.036   | 0.046± | 0.004   | 3.102±     | 0.288   | 0.943± | 0.077   | 0.986± | 0.061   |  |
| 190 ppm                                  | 10                | 310±     | 18     | 0.274± | 0.047   | 0.054± | 0.004** | 2.939±     | 0.100   | 0.940± | 0.068   | 0.980± | 0.044   |  |
| 380 ppm                                  | 10                | 292±     | 20*    | 0.268± | 0.028   | 0.047± | 0.005   | 2.907±     | 0.127   | 0.897± | 0.073   | 0.935± | 0.051   |  |
| 750 ppm                                  | 10                | $250\pm$ | 15**   | 0.208± | 0.037** | 0.046± | 0.005   | $2.831\pm$ | 0.054*  | 0.831± | 0.047** | 0.885± | 0.045*  |  |
| 1500 ppm                                 | 10                | 200±     | 18**   | 0.166± | 0.020** | 0.039± | 0.004** | 1.478±     | 0.295** | 0.733± | 0.058** | 0.901± | 0.291** |  |
| 3000 ppm                                 | 9                 | 140±     | 15**   | 0.103± | 0.025** | 0.041± | 0.002   | 1.151±     | 0.104** | 0.609± | 0.055** | 0.840± | 0.321** |  |

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STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE UNIT: g

# ORGAN WEIGHT:ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (14)

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| oup Name | NO. of<br>Animals | KID        | NEYS    | SPL    | EEN     | LIV         | ER      | BRA         |         |  |
|----------|-------------------|------------|---------|--------|---------|-------------|---------|-------------|---------|--|
| 0 mada   | 10                | 1.817±     | 0.102   | 0.511± | 0.040   | 7.966±      | 0.497   | 1.873±      | 0.046   |  |
| 190 ppm  | 10                | 1.774±     | 0.081   | 0.524± | 0.043   | 7.658±      | 0.595   | $1.845 \pm$ | 0.043   |  |
| 380 ppm  | 10                | 1.744±     | 0.134   | 0.485± | 0.035   | 7.643±      | 0.603   | 1.860±      | 0.037   |  |
| 750 ppm  | 10                | $1.633\pm$ | 0.103*  | 0.449± | 0.041*  | 6.718±      | 0.573** | 1.804±      | 0.038** |  |
| 1500 ppm | 10                | 1.467±     | 0.128** | 0.394± | 0.061** | $5.728\pm$  | 0.637** | 1.706±      | 0.054** |  |
| 3000 ppm | 9                 | 1.379±     | 0.205** | 0.337± | 0.064** | $4.795 \pm$ | 1.199** | 1.525±      | 0.037** |  |

APPENDIX B 8-2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE UNIT: g

## ORGAN WEIGHT:ABSOLUTE (SUMMARY) SURVIVAL ANIMALS ( 14)

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PAGE : 3

| oup Name | NO. of<br>Animals | Body     | Weight | ТНҮМ   | US      | ADRE   | NALS    | OVAR   | IES     | HEAR   | T       | LUNG   | S       |
|----------|-------------------|----------|--------|--------|---------|--------|---------|--------|---------|--------|---------|--------|---------|
| 0 mqq    | 10                | 178±     | 9      | 0.198± | 0.028   | 0.053± | 0.003   | 0.110± | 0.014   | 0.609± | 0.034   | 0.749± | 0.055   |
| 190 ppm  | 10                | 178±     | 12     | 0.198± | 0.019   | 0.053± | 0.004   | 0.107± | 0.011   | 0.631± | 0.050   | 0.749± | 0.044   |
| 380 ppm  | 10                | 170±     | 9      | 0.202± | 0.033   | 0.053± | 0.006   | 0.102± | 0.021   | 0.618± | 0.062   | 0.722± | 0.027   |
| 750 ppm  | 10                | $154\pm$ | 9**    | 0.175± | 0.026   | 0.048± | 0.005   | 0.093± | 0.009   | 0.632± | 0.113   | 0.741± | 0.071   |
| 1500 ppm | 10                | $130\pm$ | 9**    | 0.146± | 0.020** | 0.044± | 0.005** | 0.057± | 0.015** | 0.548± | 0.041   | 0.641± | 0.036** |
| 3000 ppm | 10                | 97±      | 6**    | 0.096± | 0.025** | 0.042± | 0.005** | 0.042± | 0.004** | 0.475± | 0.049** | 0.593± | 0.031** |

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STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE UNIT: g

### ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (14)

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Group Name SPLEEN NO. of KIDNEYS LIVER BRAIN Animals 0 ppm 10 1.147± 0.045 0.357± 0.054 4.069± 0.226  $1.725 \pm 0.058$ 190 ppm 10 1.177± 0.096  $0.355 \pm 0.023$ 4.116± 0.272  $1.725 \pm 0.040$ 380 ppm 10 1.133± 0.042 0.345± 0.026 3.963± 0.274 1.714± 0.023 750 ppm 10 1.138± 0.072 0.341± 0.038 3.802± 0.226  $1.687 \pm 0.035$ 

1500 ppm 10 1.042± 0.058\*\* 0.280± 0.025\*\* 3.517± 0.266\*\* 1.607± 0.033\*\* 3000 ppm 10 1.066± 0.043\* 0.256± 0.030\*\* 3.043± 0.204\*\* 1.463± 0.032\*\* Significant difference ;  $*: P \leq 0.05$  $**: P \leq 0.01$ Test of Dunnett (HCL040)

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APPENDIX B 8-3

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOSUE : MALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE UNIT: g

## ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (14)

| bup Name | NO. of<br>Animals | Body Weight | THYMUS       | ADRENALS     | TESTES       | HEART        | LUNGS        |  |
|----------|-------------------|-------------|--------------|--------------|--------------|--------------|--------------|--|
| maa 0    | 10                | 33.0± 1.7   | 0.039± 0.009 | 0.009± 0.002 | 0.206± 0.021 | 0.147± 0.012 | 0.152± 0.008 |  |
| 300 ppm  | 10                | 27.9± 1.7** | 0.030± 0.006 | 0.008± 0.002 | 0.191± 0.025 | 0.141± 0.011 | 0.151± 0.012 |  |
| 440 ppm  | 10                | 26.3± 1.7** | 0.032± 0.007 | 0.008± 0.003 | 0.194± 0.020 | 0.146± 0.017 | 0.152± 0.010 |  |
| 670 ppm  | 10                | 25.0± 0.8** | 0.035± 0.006 | 0.008± 0.002 | 0.191± 0.030 | 0.138± 0.011 | 0.152± 0.006 |  |
| 1000 ppm | 8                 | 25.1± 1.1** | 0.036± 0.007 | 0.009± 0.002 | 0.171± 0.024 | 0.135± 0.009 | 0.154± 0.007 |  |
| 1500 ppm | 0                 | -           | -            | -            | -            | -            |              |  |

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STUDY NO. : 0192 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE UNIT: g

| 10 |               |                                                      |                                                                     |                                                                                                         |                                                                                                                                 |                                                                                                                                                                     |                                                                                                                                                                                                     |                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                     |
|----|---------------|------------------------------------------------------|---------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    | $0.455 \pm$   | 0.032                                                | 0.046±                                                              | 0.006                                                                                                   | 1.189±                                                                                                                          | 0.077                                                                                                                                                               | 0.453±                                                                                                                                                                                              | 0.014                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                     |
| 10 | 0.602±        | 0.538                                                | 0.047±                                                              | 0.010                                                                                                   | 1.103±                                                                                                                          | 0.089                                                                                                                                                               | 0.454±                                                                                                                                                                                              | 0.016                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                     |
| 10 | 0.428±        | 0.030                                                | 0.047±                                                              | 0.006                                                                                                   | 1.105±                                                                                                                          | 0.086                                                                                                                                                               | 0.444±                                                                                                                                                                                              | 0.011                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                     |
| 10 | 0.418±        | 0.033                                                | 0.043±                                                              | 0.005                                                                                                   | 1.071±                                                                                                                          | 0.060**                                                                                                                                                             | 0.444±                                                                                                                                                                                              | 0.010                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                     |
| 8  | $0.420\pm$    | 0.040                                                | 0.043±                                                              | 0.006                                                                                                   | 1,067±                                                                                                                          | 0.068**                                                                                                                                                             | 0.430±                                                                                                                                                                                              | 0.010**                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                     |
| 0  | . –           |                                                      | -                                                                   |                                                                                                         | -                                                                                                                               |                                                                                                                                                                     | -                                                                                                                                                                                                   |                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                     |
| ]  | 10<br>10<br>8 | 10     0.428±       10     0.418±       8     0.420± | 10 $0.428 \pm$ $0.030$ 10 $0.418 \pm$ $0.033$ 8 $0.420 \pm$ $0.040$ | 10 $0.428 \pm$ $0.030$ $0.047 \pm$ 10 $0.418 \pm$ $0.033$ $0.043 \pm$ 8 $0.420 \pm$ $0.040$ $0.043 \pm$ | 10 $0.428 \pm$ $0.030$ $0.047 \pm$ $0.006$ 10 $0.418 \pm$ $0.033$ $0.043 \pm$ $0.005$ 8 $0.420 \pm$ $0.040$ $0.043 \pm$ $0.006$ | 10 $0.428 \pm$ $0.030$ $0.047 \pm$ $0.006$ $1.105 \pm$ 10 $0.418 \pm$ $0.033$ $0.043 \pm$ $0.005$ $1.071 \pm$ 8 $0.420 \pm$ $0.040$ $0.043 \pm$ $0.006$ $1.067 \pm$ | 10 $0.428 \pm$ $0.030$ $0.047 \pm$ $0.006$ $1.105 \pm$ $0.086$ 10 $0.418 \pm$ $0.033$ $0.043 \pm$ $0.005$ $1.071 \pm$ $0.060 * *$ 8 $0.420 \pm$ $0.040$ $0.043 \pm$ $0.006$ $1.067 \pm$ $0.068 * *$ | 10 $0.428 \pm$ $0.030$ $0.047 \pm$ $0.006$ $1.105 \pm$ $0.086$ $0.444 \pm$ 10 $0.418 \pm$ $0.033$ $0.043 \pm$ $0.005$ $1.071 \pm$ $0.060 * *$ $0.444 \pm$ 8 $0.420 \pm$ $0.040$ $0.043 \pm$ $0.006$ $1.067 \pm$ $0.068 * *$ $0.430 \pm$ | 10 $0.428 \pm$ $0.030$ $0.047 \pm$ $0.006$ $1.105 \pm$ $0.086$ $0.444 \pm$ $0.011$ 10 $0.418 \pm$ $0.033$ $0.043 \pm$ $0.005$ $1.071 \pm$ $0.060 * *$ $0.444 \pm$ $0.010$ 8 $0.420 \pm$ $0.040$ $0.043 \pm$ $0.006$ $1.067 \pm$ $0.068 * *$ $0.430 \pm$ $0.010 * *$ | 10 $0.428 \pm$ $0.030$ $0.047 \pm$ $0.006$ $1.105 \pm$ $0.086$ $0.444 \pm$ $0.011$ 10 $0.418 \pm$ $0.033$ $0.043 \pm$ $0.005$ $1.071 \pm$ $0.060 * *$ $0.444 \pm$ $0.010$ 8 $0.420 \pm$ $0.040$ $0.043 \pm$ $0.006$ $1.067 \pm$ $0.068 * *$ $0.430 \pm$ $0.010 * *$ | 10 $0.428 \pm$ $0.030$ $0.047 \pm$ $0.006$ $1.105 \pm$ $0.086$ $0.444 \pm$ $0.011$ 10 $0.418 \pm$ $0.033$ $0.043 \pm$ $0.005$ $1.071 \pm$ $0.060 * *$ $0.444 \pm$ $0.010$ 8 $0.420 \pm$ $0.040$ $0.043 \pm$ $0.006$ $1.067 \pm$ $0.068 * *$ $0.430 \pm$ $0.010 * *$ |

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APPENDIX B 8-4

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOSUE : FEMALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE UNIT: g

## ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (14)

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PAGE : 3

| oup Name | NO. of<br>Animals | Body Weight | THYMUS       | ADRENALS     | OVARIES      | HEART          | LUNGS        |
|----------|-------------------|-------------|--------------|--------------|--------------|----------------|--------------|
| 0 ppm    | 8                 | 23.3± 1.9   | 0.037± 0.009 | 0.011± 0.004 | 0.024± 0.009 | 0.129± 0.005   | 0.147± 0.010 |
| 300 ppm  | 10                | 21.6± 1.3*  | 0.040± 0.007 | 0.010± 0.004 | 0.024± 0.009 | 0.119± 0.011*  | 0.149± 0.015 |
| 440 ppm  | 10                | 21.4± 1.2*  | 0.040± 0.010 | 0.011± 0.003 | 0.023± 0.005 | 0.119± 0.008*  | 0.146± 0.012 |
| 670 ppm  | 10                | 20.8± 1.1** | 0.042± 0.006 | 0.009± 0.003 | 0.021± 0.005 | 0.116± 0.006** | 0.146± 0.015 |
| 1000 ppm | 9                 | 20.5± 0.9** | 0.046± 0.007 | 0.009± 0.002 | 0.022± 0.006 | 0.115± 0.009** | 0.143± 0.011 |
| 1500 ppm | 0                 | -           | -            | -            | -            | -              | -            |

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE UNIT: g

### ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (14)

Group Name NO. of KIDNEYS SPLEEN LIVER BRAIN Animals 0 ppm 8 0.316± 0.017 0.053± 0.006 0.956± 0.109 0.470± 0.012 300 ppm 10  $0.298 \pm 0.015$ 0.054± 0.009 0.948± 0.060 0.460± 0.019 440 ppm 10 0.297± 0.020 0.049± 0.008 0.958± 0.076 0.451± 0.008\* 670 ppm 10 0.290± 0.013\*\* 0.047± 0.009 0.942± 0.075 0.435± 0.012\*\* 1000 ppm 9 0.301± 0.020 0.043± 0.004\* 0.952± 0.053 0.415± 0.014\*\* 1500 ppm 0 \_ \_ \_ ----Significant difference ;  $*: P \leq 0.05$ \*\* : P ≦ 0.01 Test of Dunnett (HCL040)

BAIS 2

#### PAGE: 4

APPENDIX B 9-1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE (THIRTEEN-WEEK STUDY) STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE UNIT: %

#### ORGAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS (14)

-----

Group Name NO. of Body Weight THYMUS ADRENALS TESTES HEART LUNGS Animals (g) mqq 0 10 316± 19  $0.081 \pm 0.009$  $0.015 \pm 0.002$  $0.982 \pm 0.087$  $0.298 \pm 0.014$  $0.312 \pm 0.014$ 190 ppm 10 310± 18  $0.088 \pm 0.010$ 0.017± 0.002\*  $0.951 \pm 0.060$  $0.304 \pm 0.018$  $0.317 \pm 0.015$ 380 ppm 10 292± 20\*  $0.092 \pm 0.007$  $0.016 \pm 0.002$ 0.999± 0.059  $0.308 \pm 0.016$  $0.321 \pm 0.016$ 750 ppm 10 250土 15\*\*  $0.083 \pm 0.012$ 0.019± 0.002\*\* 1.136± 0.071\*\* 0.333± 0.016\*\* 0.354± 0.014\* 1500 ppm 10 200土 18\*\*  $0.083 \pm 0.007$ 0.020± 0.002\*\* 0.738± 0.117\*\* 0.368± 0.022\*\* 0.451± 0.134\*\* 3000 ppm 9 140土 15\*\*  $0.073 \pm 0.014$ 0.030± 0.004\*\* 0.825± 0.076\*\* 0.435± 0.014\*\* 0.599± 0.211\*\* Significant difference ;  $*: P \leq 0.05$ \*\* : P ≦ 0.01 Test of Dunnett

(HCL042)

BAIS 2

PAGE: 1

STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE UNIT: %

#### ORGAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS (14)

Group Name NO. of KIDNEYS SPLEEN LIVER BRAIN Animals 0 ppm 10  $0.575 \pm 0.016$  $0.161 \pm 0.009$  $2.521 \pm 0.089$  $0.594 \pm 0.031$ 190 ppm 10  $0.573 \pm 0.017$  $0.170 \pm 0.015$  $2.471 \pm 0.102$  $0.597 \pm 0.029$ 380 ppm 10  $0.598 \pm 0.031$  $0.166 \pm 0.007$  $2.621 \pm 0.144$  $0.640 \pm 0.046$ 

750 ppm 10 0.653± 0.022\* 0.179± 0.009\*  $2.686 \pm 0.136$ 0.723± 0.036\* • 1500 ppm 10 0.736± 0.057\*\* 0.197± 0.019\*\* 2.865± 0.157\*\* 0.859± 0.073\*\* 3000 ppm 9 0.984土 0.104\*\* 0.239± 0.029\*\* 3.409± 0.702\*\* 1.099± 0.114\*\*

Significant difference ;  $*: P \leq 0.05$   $**: P \leq 0.01$ 

Test of Dunnett

(HCL042)

BAIS 2

#### PAGE: 2

APPENDIX B 9-2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE UNIT: %

#### ORGAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS (14)

Group Name NO. of Body Weight THYMUS ADRENALS OVARIES HEART LUNGS Animals (g) 0 ppm 10 178± 9  $0.111 \pm 0.012$  $0.030 \pm 0.003$  $0.062 \pm 0.007$  $0.342 \pm 0.016$  $0.421 \pm 0.036$ 190 ppm 10 178± 12 0.112± 0.010  $0.030 \pm 0.002$  $0.060 \pm 0.003$  $0.355 \pm 0.031$  $0.421 \pm 0.019$ 380 ppm 10 170± 9  $0.118 \pm 0.015$  $0.031 \pm 0.003$  $0.060 \pm 0.010$  $0.365 \pm 0.033$  $0.426 \pm 0.018$ 750 ppm 10  $154\pm$ 9\*\*  $0.113 \pm 0.013$  $0.031 \pm 0.004$ 0.061± 0.006 0.411± 0.068\*\* 0.483± 0.055\* 1500 ppm 10  $130\pm$ 9\*\*  $0.112 \pm 0.013$  $0.034 \pm 0.003 *$ 0.044± 0.010\*\* 0.423± 0.040\*\* 0.493± 0.022\*\* 3000 ppm 10 97± 6\*\* 0.099± 0.026 0.043± 0.004\*\* 0.043± 0.005\*\* 0.490± 0.029\*\* 0.613± 0.036\*\*

Significant difference ;  $*: P \leq 0.05$   $**: P \leq 0.01$ 

Test of Dunnett

(HCL042)

BAIS 2

PAGE : 3

STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE UNIT: %

#### ORGAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS (14)

Group Name KIDNEYS NO. of SPLEEN LIVER BRAIN Animals 0 ppm 10  $0.644 \pm 0.031$  $0.200 \pm 0.022$  $2.284 \pm 0.093$  $0.970 \pm 0.063$ 190 ppm 10  $0.661 \pm 0.024$  $0.199 \pm 0.007$  $2.312 \pm 0.059$  $0.972 \pm 0.059$ 380 ppm 10  $0.669 \pm 0.030$  $0.203 \pm 0.013$  $2.334 \pm 0.064$  $1.013 \pm 0.052$ 750 ppm 10 0.740± 0.028\*\* 0.221± 0.018\* 2.472± 0.074\*\* 1.099土 0.053\*\*

 1500 ppm
 10
  $0.802 \pm 0.043 **$   $0.215 \pm 0.016$   $2.701 \pm 0.082 **$   $1.238 \pm 0.071 **$  

 3000 ppm
 10
  $1.103 \pm 0.064 **$   $0.264 \pm 0.020 **$   $3.141 \pm 0.110 **$   $1.515 \pm 0.090 **$  

 Significant difference ;  $*: P \leq 0.05$   $**: P \leq 0.01$  Test of Dunnett

(HCL042)

BAIS 2

PAGE: 4

APPENDIX B 9-3

ORGAN WEIGHT, RELATIVE : SUMMARY, MOSUE : MALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE UNIT: %

## ORGAN WEIGHT:RELATIVE (SUMMARY). SURVIVAL ANIMALS (14)

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| up Name  | NO. of<br>Animals | Body Weight<br>(g) | THYMUS       | ADRENALS     | TESTES         | HEART          | LUNGS          |  |
|----------|-------------------|--------------------|--------------|--------------|----------------|----------------|----------------|--|
| 0 ppm    | 10                | 33.0± 1.7          | 0.117± 0.023 | 0.028± 0.007 | 0.623± 0.052   | 0.445± 0.033   | 0.463± 0.020   |  |
| .300 ppm | 10                | 27.9± 1.7**        | 0.109± 0.021 | 0.030± 0.007 | 0.685± 0.073   | 0.505± 0.038** | 0.540± 0.033** |  |
| 440 ppm  | 10                | 26.3± 1.7**        | 0.120± 0.022 | 0.031± 0.011 | 0.743± 0.099*  | 0.556± 0.049** | 0.579± 0.037** |  |
| 670 ppm  | 10                | 25.0± 0.8**        | 0.138± 0.020 | 0.033± 0.008 | 0.764± 0.112** | 0.552± 0.041** | 0.610± 0.035** |  |
| 1000 ppm | 8                 | 25.1± 1.1**        | 0.144± 0.030 | 0.036± 0.005 | 0.683± 0.094   | 0.538± 0.042** | 0.613± 0.037** |  |
| 1500 ppm | 0                 | -                  | -            | -            | -              | -              | -              |  |

(HCL042)

BAIS 2

PAGE: 1

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE UNIT: %

#### ORGAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS (14)

PAGE: 2 Group Name NO. of KIDNEYS SPLEEN LIVER BRAIN Animals 0 ppm 10  $1.382 \pm 0.085$ 0.139± 0.014  $3.607 \pm 0.192$  $1.375 \pm 0.059$ 300 ppm 10  $2.170 \pm 1.973 *$ 0.167± 0.033\* 3.949± 0.203\*\*  $1.631 \pm 0.082$ 440 ppm 10 1.629± 0.091\*\* 0.179± 0.017\*\* 4.197± 0.103\*\*  $1.694 \pm 0.108 **$ 670 ppm 10 1.674± 0.116\*\* 0.172± 0.019\*\* 4.289± 0.179\*\* 1.781± 0.037\*\* 1000 ppm 8 1.676± 0.181\*\* 0.170± 0.021\* 4.251± 0.187\*\*  $1.717 \pm 0.072 **$ 1500 ppm 0 \_ -----Significant difference ;  $*: P \leq 0.05$ \*\* : P ≦ 0.01 Test of Dunnett (HCL042) BAIS 2

APPENDIX B 9-4

ORGAN WEIGHT, RELATIVE : SUMMARY, MOSUE : FEMALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE UNIT: %

## ORGAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS (14)

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PAGE : 3

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| oup Name    | NO. of<br>Animals | Body Weight<br>(g) | THYMUS         | ADRENALS     | OVARIES       | HEART        | LUNGS        | ,<br>, |
|-------------|-------------------|--------------------|----------------|--------------|---------------|--------------|--------------|--------|
| 0 ppm       | 8                 | 23.3± 1.9          | 0.159± 0.035   | 0.049± 0.018 | 0.101± 0.035  | 0.558± 0.040 | 0.634± 0.057 |        |
| 300 ppm     | 10                | 21.6± 1.3*         | 0.185± 0.030   | 0.048± 0.018 | 0.113± 0.038  | 0.551± 0.043 | 0.689± 0.067 |        |
| 440 ppm     | 10                | 21.4± 1.2*         | 0.187± 0.046   | 0.050± 0.012 | 0.106± 0.024  | 0.558± 0.049 | 0.683± 0.048 |        |
| 670 ppm     | 10                | 20.8± 1.1**        | 0.200± 0.026*  | 0.045± 0.016 | 0.103± 0.024  | 0.557± 0.032 | 0.702± 0.075 |        |
| 1000 ppm    | 9                 | 20.5± 0.9**        | 0.226± 0.031** | 0.045± 0.009 | 0.108± 0.027  | 0.560± 0.042 | 0.700± 0.044 |        |
| 1500 ppm    | 0                 | -                  | -              | -            | -             | -            | -            |        |
| Significant | difference ;      | *:P≦0.05 **        | : P ≦ 0.01     | Tes          | st of Dunnett |              |              |        |
| L042)       |                   | ·                  |                |              |               |              |              |        |

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

## ORGAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS ( 14)

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UNIT: %

PAGE: 4

| up Name     | NO. of<br>Animals | KIDNEYS       | SPLEEN       | LIVER          | BRAIN        |                                       |
|-------------|-------------------|---------------|--------------|----------------|--------------|---------------------------------------|
| 0 ppm       | 8                 | 1.362± 0.097  | 0.225± 0.016 | 4.101± 0.181   | 2.028± 0.162 |                                       |
| 300 ppm     | 10                | 1.382± 0.079  | 0.249± 0.035 | 4.387± 0.144*  | 2.134± 0.125 |                                       |
| 440 ppm     | 10                | 1.389± 0.080  | 0.227± 0.029 | 4.470± 0.178** | 2.113± 0.106 |                                       |
| 670 ppm     | 10                | 1.396± 0.051  | 0.223± 0.033 | 4.532± 0.287** | 2.097± 0.089 |                                       |
| 1000 ppm    | 9                 | 1.468± 0.060* | 0.208± 0.016 | 4.653± 0.244** | 2.027± 0.070 |                                       |
| 1500 ppm    | 0                 | -             | -            | -              | -            |                                       |
| Significant | difference ;      | *:P≦0.05 **:  | P ≦ 0.01     | Test           | of Dunnett   | · · · · · · · · · · · · · · · · · · · |
| CL042)      |                   |               |              |                |              | <u></u>                               |

APPENDIX B 10-1

# HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT: MALE : DEAD AND MORIBUND ANIMALS

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0191 ANIMAL : RAT F344

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### HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0- 14W)

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REPORT TYPE : A1

SEX : MALE

PAGE: 1

| 0rgan        | Findings                   | Group Name 0 ppm<br>No. of Animals 0<br><1> <2> <3> <4><br>(%) (%) (%) (%) | 190 ppm<br>0<br><1> <2> <3> <4><br>(%) (%) (%) (%) | 380 ppm<br>0<br><1> <2> <3> <4><br>(%) (%) (%) (%) | 750 pp<br>0<br><1> <2> <3> <4><br>(%) (%) (%) (%) |
|--------------|----------------------------|----------------------------------------------------------------------------|----------------------------------------------------|----------------------------------------------------|---------------------------------------------------|
| // 9all      |                            |                                                                            |                                                    |                                                    |                                                   |
| [Hematopoie  | tic system]                |                                                                            |                                                    |                                                    |                                                   |
| spleen       | deposit of hemosiderin     | ( -) ( -) ( -) ( -)                                                        | ( -) ( -) ( -) ( -)                                | ( -) ( -) ( -) ( -)                                | ( -) ( -) ( -) ( -)                               |
| [Digestive : | system]                    |                                                                            |                                                    |                                                    |                                                   |
| liver        | necrosis:focal             | ( -) ( -) ( -)                                                             | () () ()                                           | ( -) ( -) ( -) ( -)                                | ( -) ( -) ( -) ( -)                               |
| [Reproducti  | ve system]                 |                                                                            |                                                    |                                                    |                                                   |
| testis       | atrophy                    | ( -) ( -) ( -) ( -)                                                        | ( -) ( -) ( -) ( -)                                | ( -) ( -) ( -) ( -)                                |                                                   |
| pididymis    | decrreased:sperma          | ( -) ( -) ( -) ( -)                                                        | ( -) ( -) ( -) ( -)                                | ( -) ( -) ( -) ( -)                                | ( -) ( -) ( -) ( -)                               |
| (Nervous sy  | stem]                      |                                                                            |                                                    |                                                    | ,                                                 |
| brain        | degeneration:granular cell | ( -) ( -) ( -)                                                             | ( -) ( -) ( -) ( -)                                |                                                    | ,<br><br>() () () ()                              |

(HPT150)

BAIS2

#### STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1

: MALE

SEX

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## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0- 14W)

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PAGE: 2

| Organ        | Findings                   | Group Name 1500 ppm<br>No. of Animals 0<br><1> <2> <3> <4><br>(%) (%) (%) (%) | 3000 ppm<br>1<br><1> <2> <3> <4><br>(%) (%) (%) (%)  |  |
|--------------|----------------------------|-------------------------------------------------------------------------------|------------------------------------------------------|--|
| [Hematopoiet | tic system]                |                                                                               |                                                      |  |
| spleen       | deposit of hemosiderin     | ( -) ( -) ( -) ( -)                                                           | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ |  |
| [Digestive s | system]                    |                                                                               |                                                      |  |
| liver        | necrosis:focal             | ( -) ( -) ( -) ( -)                                                           | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ |  |
| [Reproductio | ve system]                 |                                                                               |                                                      |  |
| testis       | atrophy                    | ( -) ( -) ( -) ( -)                                                           | 0 0 0 1<br>( 0) ( 0) ( 0) (100)                      |  |
| epididymis   | decrreased:sperma          | ( -) ( -) ( -) ( -)                                                           | 0 0 1 0<br>( 0) ( 0) (100) ( 0)                      |  |
| (Nervous sys | stem]                      |                                                                               |                                                      |  |
| brain        | degeneration:granular cell | ( -) ( -) ( -) ( -)                                                           | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ |  |

(HPT150)

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BAIS2

APPENDIX B 10-2

# HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : SACRIFICED ANIMALS

(THIRTEEN-WEEK STUDY)

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STUDY NO. : 0191

## ANIMAL : RAT F344

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS ( 14W)

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REPORT TYPE : A1 SEX : MALE

PAGE: 1

| 0rgan       | Findings                   | Group Name 0 ppm<br>No. of Animals 10<br><1> <2> <3> <4><br>(%) (%) (%) (%) | 190 ppm<br>10<br><1> <2> <3> <4><br>(%) (%) (%) (%) | 380 ppm<br>10<br><1> <2> <3> <4><br>(%) (%) (%) (%) | 750 pp<br>10<br><1> <2> <3> <4><br>(%) (%) (%) (%) |
|-------------|----------------------------|-----------------------------------------------------------------------------|-----------------------------------------------------|-----------------------------------------------------|----------------------------------------------------|
| [Respirator | v system]                  |                                                                             |                                                     |                                                     | · · · · · · · · · · · · · · · · · · ·              |
| ung         | congestion                 | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     |
| Hematopoie  | tic system]                |                                                                             |                                                     |                                                     |                                                    |
| spleen      | deposit of hemosiderin     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     |
| Digestive : | system]                    |                                                                             |                                                     |                                                     |                                                    |
| iver        | herniation                 | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>(0)(0)(0)(0)                            |
| Urinary sy  | stem]                      |                                                                             |                                                     |                                                     |                                                    |
| idney       | easinaphilic bady          | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                        | 2 5 3 0<br>(20)(50)(30)(0)                          | 0 5 5 0<br>(0)(50)(50)(0)                           | 3 5 2 0<br>(30)(50)(20)(0)                         |
| Endocrine : | system]                    |                                                                             |                                                     |                                                     |                                                    |
| oituitary   | cyst                       | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                        | 2 0 0 0<br>(20)(0)(0)(0)                            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     |
| adrenal     | fatty change               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     |
| [Reproducti | ve system]                 |                                                                             |                                                     |                                                     |                                                    |
| testis      | atrophy                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     |
| Significant | : difference; *:P≦0.05 **: | P ≦ 0.01 Test of Chi Square <1>:Sligh                                       | t <2>:Moderate <                                    | 3>:Marked <4>:Severe                                |                                                    |

#### STUDY NO. : 0191 ANIMAL : RAT F344 REPORT TYPE : A1 : MALE

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS ( 14W)

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SEX

PAGE: 2

| <u>,</u>     |                        | Group Name 1500 ppm<br>No. of Animals 10<br><1> <2> <3> <4> | 3000 ppm<br>9<br><1> <2> <3> <4>                      |
|--------------|------------------------|-------------------------------------------------------------|-------------------------------------------------------|
| )rgan        | Findings               |                                                             | (%) (%) (%)                                           |
| Respiratory  | system]                |                                                             |                                                       |
| ung          | congestion             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                              | 1 0 0 0<br>(11) (0) (0) (0)                           |
| llematopoiet | ic system]             |                                                             |                                                       |
| spleen       | deposit of hemosiderin | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                              | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
| Digestive s  | ystem]                 |                                                             |                                                       |
| iver         | herniation             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                              | 0 0 0 0 (0) (0) (0)                                   |
| [Urinary sys | tem]                   |                                                             |                                                       |
| tidney       | easinaphilic body      | 6 2 0 0 *<br>(60) (20) (0) (0)                              | 0 0 0 0 **<br>( 0) ( 0) ( 0) ( 0)                     |
| [Endocrine s | ystem]                 |                                                             |                                                       |
| pituitary    | cyst                   | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |
| adrena L     | fatty change           | 6 0 0 0 *<br>(60) (0) (0) (0)                               | 8 1 0 0 **<br>(89) (11) (0) (0)                       |
| [Reproductiv | e system]              |                                                             |                                                       |
| testis       | atrophy                | 0 5 3 1 **<br>( 0) ( 50) ( 30) ( 10)                        | 0 4 5 0 **<br>( 0) ( 44) ( 56) ( 0)                   |

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|                                 | Group Name 0 ppm<br>No. of Animals 10   | 190 ppm<br>10                  | 380 ppm<br>10                      | 750 pp<br>10                           |
|---------------------------------|-----------------------------------------|--------------------------------|------------------------------------|----------------------------------------|
| gan Findings                    | <1> <2> <3> <4 (%) (%) (%) (%) (%)      |                                | <1> <2> <3> <4><br>(%) (%) (%) (%) | <1> <2> <3> <4><br>(%) (%) (%) (%) (%) |
| eproductive system]             |                                         |                                |                                    |                                        |
| edema                           | 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0          |
| pididymis decrreased:sperma     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |
| ieruaus system]                 |                                         |                                |                                    |                                        |
| rain degeneration:granular cell | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0           |                                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |

STUDY NO. : 0191 ANIMAL : RAT F344

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS ( 14W)

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| REPORT TYPE<br>SEX | : A1<br>: MALE                       |                                                                                                                                                                                                        | PAGE : 4 |
|--------------------|--------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|
| 0rgan              | Findings                             | Group Name       1500 ppm       3000 ppm         No. of Animals       10       9         <1><2><3><4><       <1><2><3><4>         (%)       (%)       (%)       (%)       (%)                          |          |
| [Reproduction      | ue system]                           |                                                                                                                                                                                                        |          |
| testis             | edema                                | 8       0       1       0 **       4       0       0       0         (80)       (0)       (10)       (0)       (44)       (0)       (0)       (0)                                                      |          |
| epididymis         | decrreased:sperma                    | 0 0 8 0 ** 0 0 9 0 **<br>( 0) ( 0) ( 80) ( 0) ( 0) ( 0) ( 100) ( 0)                                                                                                                                    |          |
| [Nervous sys       | stem]                                |                                                                                                                                                                                                        |          |
| brain              | deseneration:granular cell           | 0       0       0       2       0       0         (       0)       (       0)       (       0)       (       0)         (       0)       (       0)       (       0)       (       0)       (       0) |          |
| Significant        | difference; $*: P \leq 0.05$ $**: P$ | ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe                                                                                                                                |          |
| (HPT150)           |                                      |                                                                                                                                                                                                        | BAIS2    |

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# HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS ( 14W)

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STUDY NO. : 0191

ANIMAL : RAT F344

APPENDIX B 10-3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : SACRIFICED ANIMALS

(THIRTEEN-WEEK STUDY)

# STUDY NO. : 0191

## ANIMAL : RAT F344

#### REPORT TYPE : A1 SEX : FEMALE

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS ( 14W)

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PAGE: 5

| )mann             | Rinding                                   |                           | 190 ppm<br>10<br>4> <1> <2> <3> <4> | 380 ppm<br>10<br><1> <2> <3> <4> | 750 pp<br>10<br><1> <2> <3> <4> |
|-------------------|-------------------------------------------|---------------------------|-------------------------------------|----------------------------------|---------------------------------|
| Drgan             | Findings                                  | (%) (%) (%) (             | %) (%) (%) (%)                      | (%) (%) (%) (%)                  | (%) (%) (%)                     |
| [Hematopoietic    | system]                                   |                           |                                     |                                  |                                 |
| oone marrow       | granulation                               | 2 0 0<br>(20)(0)(0)(      | 0 2 0 0 0<br>0) (20) (0) (0) (0)    | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | 1 3 0 0<br>(10)(30)(0)(0)       |
| spleen            | deposit of hemosiderin                    | 0 0 0<br>( 0) ( 0) ( 0) ( | 0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0) | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
| Digestive sys     | tem]                                      |                           |                                     |                                  |                                 |
| Live <del>r</del> | herniation                                | 1 0 0<br>(10) (0) (0) (   | 0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0) | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
| Urinary system    | m]                                        |                           |                                     |                                  |                                 |
| idney             | mineralization:cortico-medullary junction | 8 0 0<br>(80)(0)(0)(      | 0 8 0 0 0<br>0) (80)(0)(0)(0)       | 6 0 0 0<br>(60)(0)(0)(0)         | 4 0 0 0<br>(40)(0)(0)(0)        |
| Endocrine sys     | tem]                                      |                           |                                     |                                  |                                 |
| ituitary          | cyst                                      | 0 0 0<br>( 0) ( 0) ( 0) ( | 0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0) | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(10) (0) (0) (0)     |
|                   | Rathke pouch                              | 0 0 0<br>( 0) ( 0) ( 0) ( | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)    | 1 0 0 0<br>(10) (0) (0) (0)      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
| adrenal           | fatty change                              | 0 0 0<br>( 0) ( 0) ( 0) ( | 0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0) | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(10) (0) (0) (0)     |
| Special sense     | organs/appandage]                         |                           |                                     |                                  |                                 |
| Harder gl         | lymphocytic infiltration                  | 0 0 0<br>( 0) ( 0) ( 0) ( | 0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0) | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(10)(0)(0)(0)        |

| SEX :          | FEMALE                                    |                                            |                                              |                                                      | <br>PAGE : |
|----------------|-------------------------------------------|--------------------------------------------|----------------------------------------------|------------------------------------------------------|------------|
| Organ          | Findings                                  | Group Name<br>No. of Animals<br><1><br>(%) | 1500 ppm<br>10<br><2> <3> <4><br>(%) (%) (%) | 3000 ppm<br>10<br><1> <2> <3> <4><br>(%) (%) (%) (%) |            |
| [Hematopoietic | c system]                                 |                                            |                                              |                                                      |            |
| bone marrow    | granulation                               |                                            | 1 0 0<br>(10) (0) (0)                        | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     |            |
| spleen         | deposit of hemosiderin                    | 0                                          | 0 0 0<br>( 0) ( 0) ( 0)                      | 2 0 0 0<br>(20)(0)(0)(0)                             |            |
| [Digestive sys | stem]                                     |                                            |                                              |                                                      |            |
| liver          | herniation                                | 1 (10)                                     | 0 0 0<br>( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |            |
| [Urinary syste | əm]                                       |                                            |                                              |                                                      |            |
| kidney         | mineralization:cortico-medullary junction | 0                                          | 0 0 0 ***<br>( 0) ( 0) ( 0)                  | 3 0 0 0<br>(30)(0)(0)(0)                             |            |
| [Endocrine sys | stem]                                     |                                            |                                              |                                                      |            |
| pituitary      | cyst                                      | 0<br>( 0)                                  | 0 0 0<br>( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |            |
|                | Rathke pouch                              | 0<br>( 0)                                  | 0 0 0<br>( 0) ( 0) ( 0)                      | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ |            |
| adrenal        | fatty change                              | ( 90)<br>9                                 | 0 0 0 **<br>(0)(0)(0)                        | 10 0 0 0 **<br>(100) ( 0) ( 0) ( 0)                  |            |
| [Special sens  | e organs/appandage]                       |                                            |                                              |                                                      |            |
| Harder gl      | lymphocytic infiltration                  | 1<br>(10)                                  | 0 0 0<br>( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |            |

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS ( 14W)

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Significant difference ; \* : P  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Narked <4>:Severe PAGE: 6

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REPORT TYPE : A1

# APPENDIX B 10-4

# HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY MOSUE : MALE : DEAD AND MORIBUND ANIMALS (THIRTEEN-WEEK STUDY)

## STUDY NO. : 0192 ANIMAL : MOUSE BDF1

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#### REPORT TYPE : A1 SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0- 14W)

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PAGE : 1

|              |                         | Group Name 0 ppm<br>No. of Animals 0 | 300 ppm<br>0                           | 440 ppm<br>0                           | 670 ppm<br>0                           |  |
|--------------|-------------------------|--------------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|--|
| )rgan        | Findings                | <1><2><3><4>       (%)     (%)       | <1> <2> <3> <4><br>(%) (%) (%) (%) (%) | <1> <2> <3> <4><br>(%) (%) (%) (%) (%) | <1> <2> <3> <42<br>(%) (%) (%) (%) (%) |  |
| Respiratory  | system]                 |                                      |                                        |                                        |                                        |  |
| ung          | congestion              | ( -) ( -) ( -)                       | ( -) ( -) ( -) ( -)                    | ( -) ( -) ( -) ( -)                    | ( -) ( -) ( -) ( -)                    |  |
| [Hematopoiet | ic system]              |                                      |                                        |                                        |                                        |  |
| spleen       | deposit of melanin      | ( -) ( -) ( -) ( -)                  | ( -) ( -) ( -) ( -)                    | ( -) ( -) ( -) ( -)                    | ( -) ( -) ( -) ( -                     |  |
| Digestive s  | ystem]                  |                                      |                                        |                                        |                                        |  |
| liver        | necrosis:central        | ( -) ( -) ( -) ( -)                  | ( -) ( -) ( -) ( -)                    | ( -) ( -) ( -) ( -)                    | ( -) ( -) ( -) ( -                     |  |
|              | deposit of calcium      | ( -) ( -) ( -) ( -)                  | ( -) ( -) ( -) ( -)                    | ( -) ( -) ( -) ( -)                    | ( -) ( -) ( -) ( -                     |  |
|              | vacuolic change:central | ( -) ( -) ( -) ( -)                  | ( -) ( -) ( -) ( -)                    | ( -) ( -) ( -) ( -)                    | ( -) ( -) ( -) ( -                     |  |
| [Urinary sys | tem]                    |                                      |                                        |                                        |                                        |  |
| kidney       | hydronephros i s        | ( -) ( -) ( -) ( -)                  | ( -) ( -) ( -) ( -)                    | ( -) ( -) ( -) ( -)                    |                                        |  |
|              | tubular necrosis        | ( -) ( -) ( -) ( -)                  | ( -) ( -) ( -) ( -)                    | ( -) ( -) ( -) ( -)                    | <br>( -) ( -) ( -) ( -                 |  |
| [Reproductiv | e system]               |                                      |                                        |                                        |                                        |  |
| epididymis   | spermatogenic granuloma | ( -) ( -) ( -)                       | <br>( -) ( -) ( -) ( -)                | ( -) ( -) ( -) ( -)                    | <br>( -) ( -) ( -) ( -                 |  |

(HPT150)

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0- 14W)

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PAGE : 2

| 0rgan        | Findings                | Group Name 1000 ppm<br>No. of Animals 2<br><1> <2> <3> <4><br>(%) (%) (%) (%) | 1500 ppm<br>10<br><1> <2> <3> <4><br>(%) (%) (%) |  |
|--------------|-------------------------|-------------------------------------------------------------------------------|--------------------------------------------------|--|
| [Respiratory | system]                 |                                                                               |                                                  |  |
| lung         | congestion              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                | 1 0 0 0<br>(10) (0) (0) (0)                      |  |
| [Hematopoiet | ic system]              |                                                                               |                                                  |  |
| spleen       | deposit of melanin      | 1 0 0 0<br>(50)(0)(0)(0)                                                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   |  |
| [Digestive s | ystem]                  |                                                                               |                                                  |  |
| liver        | necrosis:central        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                | 1 1 3 1<br>(10) (10) (30) (10)                   |  |
|              | deposit of calcium      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                | 2 0 0 0<br>(20) (0) (0) (0)                      |  |
|              | Vacuolic change:central | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                | 0 0 0 1<br>( 0) ( 0) ( 0) ( 10)                  |  |
| [Urinary sys | tem]                    |                                                                               |                                                  |  |
| kidney       | hydronephras i s        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                | 1 0 0 0<br>(10) (0) (0) (0)                      |  |
|              | tubular necrosis        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                | 2 0 1 0<br>(20) (0) (10) (0)                     |  |
| [Reproductiv | e system]               |                                                                               |                                                  |  |
| epididymis   | spermatogenic granuloma | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                | 1 0 0 0<br>(10)(0)(0)(0)                         |  |

(THIRTEEN-WEEK STUDY)

MOSUE : MALE : SACRIFICED ANIMALS

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

APPENDIX B 10-5

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS ( 14W)

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PAGE : 1

| Rathke pouch       1       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       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       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 <t< th=""><th>)rgan</th><th>Findings</th><th>Group Name 0 ppm<br/>No. of Animals 10<br/>&lt;1&gt; &lt;2&gt; &lt;3&gt; &lt;4&gt;<br/>(%) (%) (%) (%)</th><th>300 ppm<br/>10<br/>&lt;1&gt; &lt;2&gt; &lt;3&gt; &lt;4&gt;<br/>(%) (%) (%) (%)</th><th>440 ppm<br/>10<br/>&lt;1&gt; &lt;2&gt; &lt;3&gt; &lt;4&gt;<br/>(%) (%) (%) (%)</th><th>670 ppm<br/>10<br/>&lt;1&gt; &lt;2&gt; &lt;3&gt; &lt;42<br/>(%) (%) (%) (%)</th></t<> | )rgan          | Findings                | Group Name 0 ppm<br>No. of Animals 10<br><1> <2> <3> <4><br>(%) (%) (%) (%) | 300 ppm<br>10<br><1> <2> <3> <4><br>(%) (%) (%) (%) | 440 ppm<br>10<br><1> <2> <3> <4><br>(%) (%) (%) (%) | 670 ppm<br>10<br><1> <2> <3> <42<br>(%) (%) (%) (%) |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|-------------------------|-----------------------------------------------------------------------------|-----------------------------------------------------|-----------------------------------------------------|-----------------------------------------------------|
| (0) (0) (0) (0) (0) (10) (0) (0) (0) (0) (0) (0) (0) (0) (0) (                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | [Hematopoietic | : system]               |                                                                             |                                                     |                                                     |                                                     |
| iver       vacualic change: central       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       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       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                                                                                                                                                                                                                                                                                                                                                                                                                          | pleen          | deposit of melanin      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                              | 1 0 0 0<br>(10)(0)(0)(0)(0)                         | 3 0 0 0<br>(30)(0)(0)(0)                            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      |
| (0) (0) (0) (0) (0) (0) (0) (0) (0) (0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Digestive sys  | stem]                   |                                                                             |                                                     |                                                     |                                                     |
| kidney       hydronephrosis       0       0       0       0       0       0       1       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       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       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                                                                                                                                                                                                                                                                                                                                                                                                                          | .iver          | vacuolic change:central | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      |
| (0) (0) (0) (0) (0) (0) (0) (0) (0) (0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Urinary syste  | m]                      |                                                                             |                                                     |                                                     |                                                     |
| ituitary       cyst       1       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       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       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 <td< td=""><td>idney</td><td>hvdronephrosis</td><td>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</td><td>0 0 1 0<br/>( 0) ( 0) ( 10) ( 0)</td><td>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</td><td>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</td></td<>                                                                                                                                                                                                          | idney          | hvdronephrosis          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                              | 0 0 1 0<br>( 0) ( 0) ( 10) ( 0)                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      |
| Rathke pouch       1       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       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       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 <t< td=""><td>Endocrine sys</td><td>tem]</td><td></td><td></td><td></td><td></td></t<>                                                                                                                                                                                                                                                                                                                                          | Endocrine sys  | tem]                    |                                                                             |                                                     |                                                     |                                                     |
| (10) (0) (0) (0) (0) (0) (0) (0) (0) (0) (                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | ituitary       | oyst                    | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 3 0 0 0<br>(30)(0)(0)(0)                            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0                       |
| Reproductive system]<br>pididymis spermatogenic granuloma 1000 000 000 000 000 000                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                |                         |                                                                             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>(0)(0)(0)(0)(0)                          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0                       |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Reproductive   |                         |                                                                             |                                                     |                                                     |                                                     |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | pididymis      | spermatogenic granuloma | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                        | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 0 0 0 0 0 0 0 ( 0) ( 0)                             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0                       |

(HPT150)

BAIS2

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 : MALE SEX

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS ( 14W)

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PAGE: 2

| Organ                                                                                                       | Findings                    | Group Name 1000 ppm<br>No. of Animals 8<br><1> <2> <3> <4><br>(%) (%) (%) (%) | 1500 ppm<br>0<br><1> <2> <3> <4><br>(%) (%) (%) |    |
|-------------------------------------------------------------------------------------------------------------|-----------------------------|-------------------------------------------------------------------------------|-------------------------------------------------|----|
| [Hematopoiet                                                                                                | ic system]                  |                                                                               |                                                 |    |
| spleen                                                                                                      | deposit of melanin          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                | ( -) ( -) ( -) ( -)                             |    |
| [Digestive s                                                                                                | ystem]                      |                                                                               |                                                 |    |
| liver                                                                                                       | vacuolic change:central     | 2 0 0 0<br>(25)(0)(0)(0)                                                      | ( -) ( -) ( -)                                  |    |
| [Urinary sys <sup>.</sup>                                                                                   | tem]                        |                                                                               |                                                 |    |
| <idney< td=""><td>hydronephros i s</td><td>0 1 0 0<br/>( 0) ( 13) ( 0) ( 0)</td><td></td><td></td></idney<> | hydronephros i s            | 0 1 0 0<br>( 0) ( 13) ( 0) ( 0)                                               |                                                 |    |
| [Endocrine s:                                                                                               | ystem]                      |                                                                               |                                                 |    |
| pituitary                                                                                                   | cyst                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                | ( -) ( -) ( -) ( -)                             |    |
|                                                                                                             | Rathke pouch                |                                                                               | ( -) ( -) ( -) ( -)                             |    |
| [Reproductiv                                                                                                | e system]                   |                                                                               |                                                 |    |
| epididymis                                                                                                  | spermatogenic granuloma     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                | ( -) ( -) ( -) ( -)                             |    |
| Significant                                                                                                 | difference; *:P ≤ 0.05 **:P | ≦ 0.01 Test of Chi Square <1>:Sligh                                           | t <2>:Moderate <3>:Marked <4>:Seve              | re |
| (HPT150)                                                                                                    |                             |                                                                               |                                                 | В  |

# APPENDIX B 10-6

# HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOSUE : FEMALE : SACRIFICED ANIMALS

(THIRTEEN-WEEK STUDY))

|                                          | Group Name<br>No. of Animal |            | 8          | 0 ppm<br>B |            |            | 1          | mqq 00<br>0 |            |            | 1          | 40 ppm<br>0 |            |            |            | 670 pp<br>10 |       |
|------------------------------------------|-----------------------------|------------|------------|------------|------------|------------|------------|-------------|------------|------------|------------|-------------|------------|------------|------------|--------------|-------|
| gan Findings                             |                             | <1><br>(%) | <2><br>(%) | <3><br>(%) | <4><br>(%) | <1><br>(%) | <2><br>(%) | <3><br>(%)  | <4><br>(%) | <1><br>(%) | <2><br>(%) | <3><br>(%)  | <4><br>(%) | <1)<br>(%) |            |              |       |
| espiratory system]                       |                             |            |            |            |            |            |            |             |            |            |            |             |            |            |            |              |       |
| ng bronchiolar-alveolar cell hyperplasia | (                           | 0<br>0) (  | 0<br>0)    | 0<br>( 0)  | 0<br>( 0)  | 1<br>(10)  | 0<br>( 0)  | 0<br>( 0)   | 0<br>( 0)  | 0          | 0<br>( 0)  | 0<br>( 0)   | 0<br>( 0)  | 0<br>( 0   | ) ( 0)     | 0<br>) ( 0)  | 0     |
| ematopoietic system]                     |                             |            |            |            |            |            |            |             |            |            |            |             |            |            |            |              |       |
| oleen deposit of melanin                 | (                           | 0<br>0) (  | 0<br>( 0)   | 0<br>( 0)  | 1<br>(10)  | 0<br>( 0)  | 0<br>( 0)   | 0<br>( 0)  | 0<br>( 0   | 0<br>) ( 0 | 0<br>) ( 0)  | 0     |
| 2ndocrine system]                        |                             |            |            |            |            |            | •          |             |            |            |            |             |            |            |            |              |       |
| tuitary cyst                             | (                           | 0<br>0) (  | 0          | 0<br>( 0)   | 0<br>( 0)  | 1<br>(10)  | 0<br>( 0)  | 0<br>( 0)   | 0<br>( 0)  | 0<br>( 0   | ) ( 0)     | 0<br>) ( 0)  | 0 ( 0 |

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS ( 14W)

STUDY NO. : 0192 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 CEV

# $\sim$

| ANIMAL<br>REPORT TYPE | : 0192<br>: MOUSE BDF1<br>: A1<br>: FEMALE    | HISTOLOGICAL FINDINGS : NON-N<br>SACRIFICED ANIMALS ( 14W)                    | NEOPLASTIC LESIONS (SUMMARY)                        |            | PAGE: 4 |
|-----------------------|-----------------------------------------------|-------------------------------------------------------------------------------|-----------------------------------------------------|------------|---------|
| 0rgan                 | Findings                                      | Group Name 1000 ppm<br>No. of Animals 9<br><1> <2> <3> <4><br>(%) (%) (%) (%) | 1500 ppm<br>0<br><1> <2> <3> <4><br>(%) (%) (%) (%) |            |         |
| [Respiratory          | y system]                                     |                                                                               |                                                     |            |         |
| lung                  | bronchiolar-alveolar cell hyperplasia         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                | ( -) ( -) ( -) ( -)                                 |            |         |
| [Hematopoie           | tic system]                                   |                                                                               |                                                     |            |         |
| spleen                | deposit of melanin                            | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                          | ( -) ( -) ( -) ( -)                                 |            |         |
| [Endocrine :          | system]                                       |                                                                               |                                                     |            |         |
| pituitary             | cyst                                          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                |                                                     |            |         |
| Significant           | difference; $*: P \leq 0.05$ $**: P \leq 0.0$ | 1 Test of Chi Square <1>:Slight                                               | t <2>:Moderate <3>:Marked                           | <4>:Severe |         |
| (HPT150)              |                                               |                                                                               |                                                     | ·····      | BAIS2   |

Sec. 1

APPENDIX B 11-1

# IDENTITY AND PURITY OF METHYL CHLORIDE PERFORMED AT THE JAPAN BIOASSAY LABORATORY (THIRTEEN-WEEK STUDY)

IDENTITY AND PURITY OF METHYL CHLORIDE PERFORMED AT THE JAPANBICASSAY LABORATORY (THIRTEEN-WEEK STUDIES)

Lot no.83610

1. Spectral data

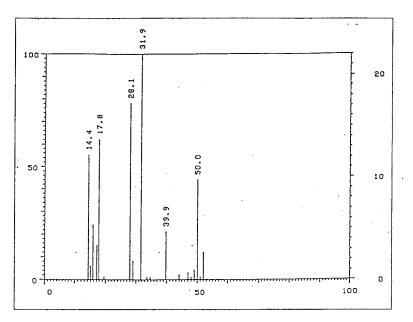
(1) Mass Spectrometry

Instrument:

Hitachi M-80B

Ionization: EI(Electron Ionization)

Ionization Voltage: 70eV



Mass Spectrum of METHYL CHLORIDE

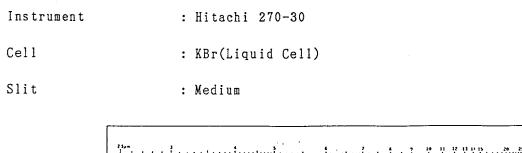
Result:

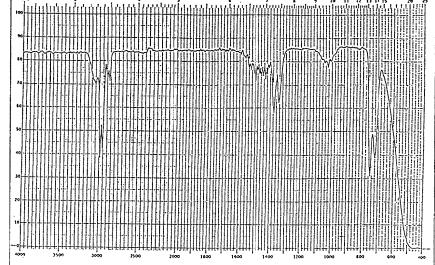
1

## Molecule Weight

| Theoretical Value | 49.99(Calculated) |
|-------------------|-------------------|
| Determined        | 50.0              |

(2) Infrared Spectrometry





Infrared Spectrum of METHYL CHLORIDE

Results

Determines : Wave Number  $(CM^{-1})$ 

 $680 \sim 780$ 960~1080 1300~1400 1420~1580 2900~3100 (Sadtler Handbook by Sadtler Research Laboratories, Inc.)

Literature Values

2. Gas Chromatography

| Instrument:         | Hewlett Packard 5890A                     |                    |
|---------------------|-------------------------------------------|--------------------|
| Column:             | Methyl Silicone(0.2mm $\phi \times 50$ m) |                    |
| Column Temperature: | 80°C                                      |                    |
| Flow Rate:          | 1 ml/min                                  |                    |
| Detector:           | FID(Hydrogen Flame Ionization)            |                    |
| Injection Volume:   | 1 µ l                                     |                    |
| Results: Only major | peak                                      |                    |
| Retention           | Retention Time<br>Relative to             | AREA<br>(percent ) |

| Retention |           | Relative to | (percent of |
|-----------|-----------|-------------|-------------|
| Peak No.  | Time(min) | Major Peak  | major peak) |
| 1         | 2.103     | 1.00        | 100         |

3. Conclusions: The result of the mass spectrum agreed with the theoretical value and the infrared spectrum agreed with the literature values. Gas chromtography indicated only the major peak.

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# APPENDIX B 11-2

# STABILITY OF METHYL CHLORIDE AT THE JAPAN BIOASSAY LABORATORY (THIRTEEN-WEEK STUDY)

STABILITY OF METHYL CHLORIDE AT THE JAPAN BIOASSAY LABORATORY(THIRTEEN-WEEK STUDIE S)

Lot no. 83610

1. Sample storage: Methyl Chloride was stored for about 13 weeks at 5°C.

2. Infrared Spectrometry

| Instrument | : Hitachi 270-30                                             |                  |
|------------|--------------------------------------------------------------|------------------|
| Cell       | : KBr(Liquid Cell)                                           |                  |
| Slit       | : Medium                                                     |                  |
| Results    | $\frac{01/23/92}{\text{Wave Number}}$<br>(CM <sup>-1</sup> ) | 05/14/92         |
|            | 700~ 780                                                     | 700~ 780         |
|            | 960~1100                                                     | 960~1100         |
|            | 1300~1400                                                    | 1300~1400        |
|            | $1420 \sim 1580$                                             | $1420 \sim 1580$ |
|            | 2900~3100                                                    | $2900 \sim 3100$ |

2.Gas Chromatography

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| Instrument:         | Hewlett Packard 5890A                     |
|---------------------|-------------------------------------------|
| Column:             | Methyl Silicone(0.2mm $\phi \times 50$ m) |
| Column Temperature: | 80° C                                     |
| Flow Rate:          | 1 ml/min                                  |
| Detector:           | FID(Hydrogen Flame Ionization)            |
| Injection Volume:   | 1 μ1                                      |

Results: Only major peak

| Date       | Retention<br>Time(min) | Retention Time<br>Relative to<br>Major Peak | Area<br>(percent of<br>Major peak) |
|------------|------------------------|---------------------------------------------|------------------------------------|
| 01/23/92 · | 2.103                  | 1.00                                        | 1 0 0                              |
| 05/14/92   | 2.102                  | 1.00                                        | 100                                |

3. Conclusions: The results of the infrared spectrum agreed with the previous determine of test values.Gas chromatography indicates only the major peak. Consequently, Methyl Chloride was stable as the chemical when stored for about 13 weeks at 5°C.

# APPENDIX B 12-1

# CONCENTRATION OF METHYL CHLORIDE IN INHALATION CHAMBER (THIRTEEN-WEEK STUDY)

|            | Concentration(ppm) |          |      |  |  |
|------------|--------------------|----------|------|--|--|
| Group Name | Mean               | ± .      | S.D. |  |  |
| Control    | 0.0                | <u>+</u> | 0.0  |  |  |
| 190ppm     | 189.7              | ±        | 1.1  |  |  |
| 380ppm     | 380.2              | 土        | 1.9  |  |  |
| 750ppm     | 748.6              | ±        | 4.6  |  |  |
| 1500ppm    | 1495.8             | <u>+</u> | 5.4  |  |  |
| 3000ppm    | 3001.3             | <u>+</u> | 14.2 |  |  |

CONCENTRATION OF METHYL CHLORIDE IN INHALATION CHAMBER (RAT : THIRTEEN-WEEK STUDY)

CONCENTRATION OF METHYL CHLORIDE IN INHALATION CHAMBER (MOUSE : THIRTEEN-WEEK STUDY)

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| Group Name | Concentration(ppm) |          |      |  |  |  |
|------------|--------------------|----------|------|--|--|--|
|            | Mean               | <u>+</u> | S.D. |  |  |  |
| Control    | 0.0                | <u>+</u> | 0.0  |  |  |  |
| 300ppm     | 299.3              | ±        | 1.5  |  |  |  |
| 440ppm     | 440.6              | ±        | 1.8  |  |  |  |
| 670ppm     | 669.7              | 土        | 2.8  |  |  |  |
| 1000ppm    | 999.1              | <u>+</u> | 5.7  |  |  |  |
| 1500ppm    | 1499.8             | <u>+</u> | 6.7  |  |  |  |

APPENDIX B 12-2

ENVIRONMENT OF INHALATION CHAMBER

(THIRTEEN-WEEK STUDY)

# ENVIRONMENT OF INHALATION CHAMBER

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(RAT : THIRTEEN-WEEK STUDY)

| roup Name | TEMPI<br>MEAN | ERATU<br>± | RE(℃)<br>S.D. | HUM]<br>MEAN | (DITY<br>± | (%)<br>S.D. | VENTILATI<br>MEAN | ION R.<br>± | ATE( 2 /min)<br>S.D. | ROOM AIR CHANGE(time/h)<br>MEAN |
|-----------|---------------|------------|---------------|--------------|------------|-------------|-------------------|-------------|----------------------|---------------------------------|
| Control   | 22.8          | +          | 0.3           | 60.6         |            | 1.8         | 010 0             |             |                      |                                 |
| 190pm     | 22.9          | _          |               |              |            |             | 212.6             | ±           | 0.6                  | 12.0                            |
| -         |               | ±          | 0.2           | 58.2         | <u>+</u>   | 0.9         | 212.5             | $\pm$       | 1.1                  | 12.0                            |
| 380pm     | 22.7          | <u>+</u>   | 0.2           | 60.2         | <u>+</u>   | 1.3         | 212.4             | <u>+</u>    | 0.5                  | 12.0                            |
| 750pm     | 22.7          | $\pm$      | 0.1           | 56.5         | $\pm$      | 0.9         | 212.0             | $\pm$       | 0.6                  | 12.0                            |
| 1500pm    | 22.8          | $\pm$      | 0.1           | 56.4         | +          | 1.2         | 212.4             |             | 0.5                  |                                 |
| 3000pm    | 22.5          | $\pm$      | 0.1           | 56.4         | ±          | 1.0         | 212.4<br>212.4    | <br>±       | 0.6                  | 12.0<br>12.0                    |

# ENVIRONMENT OF INHALATION CHAMBER

(MOUSE : THIRTEEN-WEEK STUDY)

| TEMPERATURE (°C)           |      | RE (°C)  | HUMIDITY(%) |      |          | VENTILATION RATE( 2 /min) |       | ATE( 2 /min) | ROOM AIR CHANGE(time/h) |      |
|----------------------------|------|----------|-------------|------|----------|---------------------------|-------|--------------|-------------------------|------|
| Group Name MEAN $\pm$ S.D. | MEAN | <u>±</u> | S.D.        | MEAN | ±        | S. D.                     | MEAN  |              |                         |      |
| Control                    | 21.9 | ±        | 0.1         | 59.5 | ±        | 2.3                       | 103.5 | +            | 0.3                     | 12.0 |
| 300ppm                     | 22.0 | ± .      | 0.1         | 59.8 | 土        | 1.6                       | 104.4 | ±            | 0.4                     | 12.0 |
| 440ppm                     | 21.9 | $\pm$    | 0.1         | 53.7 | $\pm$    | 1.5                       | 104.3 |              | 0.3                     | 12.0 |
| 670ppm                     | 22.6 | $\pm$    | 0.1         | 54.7 | $\pm$    | 1.0                       | 104.2 | <br>±        | 0.4                     | 12.0 |
| 1000ppm                    | 22.3 | $\pm$    | 0.1         | 54.1 | <u>+</u> | 0.9                       | 104.1 | +            | 0.4                     | 12.0 |
| 1500ppm                    | 21.6 | 土        | 0.2         | 54.3 | $\pm$    | 0.7                       | 104.1 |              | 0.3                     | 12.0 |

APPENDIX C 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

## METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

| Item                                                                                      | Method                                                              | Unit    |
|-------------------------------------------------------------------------------------------|---------------------------------------------------------------------|---------|
| Hematology                                                                                |                                                                     |         |
| Red blood cell (RBC)                                                                      | Light scattering method 1)                                          | ×10°∕µ1 |
| Hemoglobin (Hgb)                                                                          | Cyanmethemoglobin method 1)                                         | g⁄dl    |
| Hematocrit (Hct)                                                                          | Calculated as RBC $\times$ MCV $/$ 10 <sup>1)</sup>                 | %       |
| Mean corpuscular volume (MCV)                                                             | Light scattering method 1)                                          | fl      |
| Mean corpuscular hemoglobin (MCH)                                                         | Calculated as Hgb/RBC×10 $^{1)}$                                    | Pg      |
| Mean corpuscular hemoglobin                                                               | •                                                                   |         |
| concentration (MCHC)                                                                      | Calculated as Hgb/Hct $\times100^{-1}$                              | g⁄dl    |
| Platelet                                                                                  | Light scattering method 1)                                          | ×10³∕µ] |
| White blood cell (WBC)                                                                    | Light scattering method 1)                                          | ×10³∕µ1 |
| Differential WBC                                                                          | Pattern recognition method 2)                                       | %       |
|                                                                                           | (May-Grunwald-Giemsa staining)                                      |         |
| Biochemistry                                                                              |                                                                     |         |
| Total protein (TP)                                                                        | Biuret method <sup>3)</sup>                                         | g⁄dl    |
| Albumin (Alb)                                                                             | BCG method <sup>3)</sup>                                            | g⁄dl    |
| A/G ratio                                                                                 | Calculated as Alb/ (TP-Alb) 3)                                      |         |
| T-bilirubin                                                                               | Michaelson method <sup>3)</sup>                                     | mg⁄dl   |
| Glucose                                                                                   | Enzymatic method (HK·G-6-PDH) 3)                                    | mg/dl   |
| T-cholesterol                                                                             | Enzymatic method (CEH·COD·POD) 3)                                   | mg/dl   |
| Triglyceride                                                                              | Enzymatic method (GK·GPO·POD) <sup>3)</sup>                         | mg/dl   |
| Phospholipid                                                                              | Enzymatic method (PLD·COD·POD) 3)                                   | mg/dl   |
| Glutamic oxaloacetic transaminase (GOT)                                                   | Karmen method <sup>3)</sup>                                         | IU/1    |
| Glutamic pyruvic transaminase (GPT)                                                       | Karmen method <sup>3)</sup>                                         | IU/1    |
| Lactate dehydrogenase (LDH)                                                               | Wroblewski-LaDue method <sup>3)</sup>                               | IU/1    |
| Alkaline phosphatase (ALP)                                                                | GSCC method <sup>3)</sup>                                           | IU/l    |
| $\gamma$ -Glutamyl transpeptidase (G-GTP)                                                 | L- $\gamma$ -Glutamyl-p-nitroanilide substrate method <sup>3)</sup> | IU/1    |
| Creatine phosphokinase (CPK)                                                              | GSCC method <sup>3)</sup>                                           | IU/1    |
| Urea nitrogen                                                                             | Enzymatic method (Urease GLDH) 3)                                   | mg/dl   |
| Creatinine                                                                                | Jaffe method <sup>3)</sup>                                          | mg/dl   |
| Sodium                                                                                    | Flame photometry <sup>4)</sup>                                      | mEq/l   |
| Potassium                                                                                 | Flame photometry <sup>4)</sup>                                      | mEq/l   |
| Chloride                                                                                  | Coulometric titration <sup>4)</sup>                                 | mEq/l   |
| Calcium                                                                                   | 0CPC method <sup>3)</sup>                                           | mg/dl   |
| Inorganic phosphorus                                                                      | Enzymatic method (SPL·PGM·G-6-PDH) <sup>3)</sup>                    | mg/dl   |
| Urinalysis<br>pH, Protein, Glucose, Ketone body,<br>Bilirubin, Occult blood, Urobilinogen | Urinalysis reagent paper method <sup>5)</sup>                       |         |

1) Automatic blood cell analyzer (Technicon H·1 : Technicon Instruments Corporation, USA)

2) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi, Ltd., Japan)

3) Automatic analyzer (Hitachi 705 : Hitachi, Ltd., Japan)

4) Flame photometer (Hitachi 750 : Hitachi,Ltd.,Japan)

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5) Ames reagent strips for urinalysis (Multistix, Uro-Labstix : Miles Sankyo Co.,Ltd.,Japan)

APPENDIX C 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALSYS

# UNITS AND DECIMNAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

|              | TEST ITEM                           | DECIMAL PLACE | UNIT                  |
|--------------|-------------------------------------|---------------|-----------------------|
| HEMATOLOGY   | Red blood cell                      | 2             | ×10 <sup>6</sup> /µ1  |
|              | Hemoglobin                          | 1             | g/dl                  |
|              | Hematocrit                          | 1             | %                     |
|              | MCV                                 | 1             | fl                    |
|              | Platelet                            | 0             | $\times 10^3 / \mu 1$ |
|              | White blood cell<br>Differntial WBC | 2<br>0        | ×10³/µ1<br>%          |
| BIOCHEMISTRY | Total protein                       | 1             | g/dl                  |
|              | Albumin                             | 1             | g/dl                  |
|              | A/G ratio                           | 1             |                       |
|              | T-bilirubin                         | 2             | mg/dl                 |
|              | Glucose                             | 0             | mg/dl                 |
|              | T-cholesterol                       | 0             | mg/dl                 |
|              | Triglyceride                        | 0             | mg/dl                 |
|              | Phospholipid                        | 0             | mg/dl                 |
|              | GOT                                 | 0             | IU/1                  |
|              | GPT                                 | 0             | IU/1                  |
|              | $\gamma$ -GTP                       | 0             | IU/1                  |
|              | LDH                                 | 0             | IU/1                  |
|              | ALP                                 | 0             | IU/1                  |
|              | СРК                                 | 0             | IU/1                  |
|              | Urea nitrogen                       | 1             | mg/dl                 |
|              | Creatinine                          | 1             | mg/dl                 |
|              | Sodium                              | 0             | mEq/l                 |
|              | Potassium                           | 1             | mEq/l                 |
|              | Chloride                            | 0             | mEq/l                 |
|              | Calcium                             | 1             | mg/dl                 |
|              | Inorganic phosphorus                | 1             | mg/dl                 |

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