4-クロロ-2-ニトロアニリンのラットを用いた 経口投与による13週間毒性試験(混餌試験)報告書

試験番号:0745

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TABLE A 1

SURVIVAL ANIMAL NUMBERS: MALE

SURVIVAL ANIMAL NUMBERS

STUDY NO. : 0745 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] REPORT TYPE : A1 13 SEX : MALE

Group Name	Animals	Administ	ration (Wee	ks)											
	At start	0	1	2	3	4	5	6	7	8	9	10	11	12	13
mtrol	10	10/10 100. 0	10/10 100.0	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100. 0								
10 ppm	10	10/10 100. 0	10/10 100.0	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100. 0								
300 ppm	10	10/10 100. 0	10/10 100.0	10/10 100. 0	10/10 100. 0	10/10 100.0	10/10 100. 0								
000 ppm	10	10/10 100. 0	10/10 100. 0	10/10 100.0	10/10 100. 0	10/10 100.0									
mqq 00C	10	10/10 100. 0	10/10 100.0	10/10 100. 0	10/10 100. 0	10/10 100.0	10/10 100. 0								
0000 ppm	10	10/10 100.0	10/10 100.0	10/10 100.0	10/10 100. 0	10/10 100. 0	10/10 100.0	10/10 100.0	10/10 100.0	10/10 100. 0	10/10 100.0	10/10 100.0	10/10 100. 0	10/10 100. 0	10/10 100.0

Number of survival/ Number of effective animals

Survival rate(%)

(HAN360)

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TABLE A 2

SURVIVAL ANIMAL NUMBERS: FEMALE

SURVIVAL ANIMAL NUMBERS

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STUDY NO. : 0745 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] REPORT TYPE : A1 13

SEX : FEMALE															PAGE : 2
Group Name	Animals	Administ	ration (Wee	eks)											
	At start	0	1	2	3	4	5	6	7	8	9	10	11	12	13
Control	10	10/10 100. 0	10/10 100.0	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100. 0					
640 ppm	10	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100. 0							
1600 ppm	10	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100.0	10/10 100. 0							
4000 ppm	10	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100. 0							
7000 ppm	10	10/10 100. 0	10/10 100. 0	10/10 100.0	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100.0	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100.0	10/10 100. 0	10/10 100. 0
10000 ppm	10	10/10 100. 0	10/10 100.0	10/10 100.0	· 10/10 100.0	10/10 100. 0	10/10 100.0	10/10 100. 0	10/10 100. 0	10/10 100. 0	10/10 100. 0				

Number of survival/ Number of effective animals Survival rate(%)

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TABLE B 1

CLINICAL OBSERVATION: MALE

STUDY NO. : 0745 ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj] REPORT TYPE : A1 13

.

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : MALE															PAGE : 1
Clinical sign	Group Name	Admini	stration W	eek-day											
	· · · · ·	1-7	2-7	3-7	47	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7	
COLORED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
	640 ppm	0	0	0	0	8	9	10	10	10	10	10	10	10	
	1600 ppm	0	4	4	4	10	10	10	10	10	10	10	10	10	
	4000 ppm	0	7	8	8	9	10	10	10	10	10	10	10	10	
	7000 ppm	0	10	10	10	10	10	10	10	10	10	10	10	10	
		•			10			10	10	10	10	10	10	10	

COLORED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
COLONED	640 ppm	Ō	Õ	õ	õ	8	9	10	10	10	10	10	10	10
	1600 ppm	0	4	4	4	10	10	10	10	10	10	10	10	10
	4000 ppm	0	7	8	8	9	10	10	10	10	10	10	10	10
	7000 µpm	0	10	10	10	10	10	10	10	10	10	10	10	10
	10000 ppm	0	10	10	10	10	10	10	10	10	10	10	10	10
YELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
TEEDOW ONLINE	640 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	1600 µpm	10	10	10	10	10	10	10	10	10	10	10	10	10
ν, see the second se	4000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	7000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	10000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
SMALL STOOL	Control	0	0	0	0	0	0	0	0	. 0	. 0	0	0	0
	640 ppm	0	Ō	Ó	Ó	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	7000 ppm	10	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	10	0	0	0	0	0	0	0	0	0	0	0	0
OLIGO-STOOL	Control	0	. 0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	• 0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	7000 ppm	10	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	10	0	0	0	0	0	0	0	0	0	0	0	0
NON REMARKABLE	Control	10	10	10	10	10	10	10	10	10	10	10	10	10
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0 -	0	0	0
	7000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	. 0	0	0	0	0	0	0	0

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TABLE B 2

CLINICAL OBSERVATION: FEMALE

STUDY NO. : 0745 ANIMAL : RAT F344/DuCr1Cr1,j[F344/DuCr,j] REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : FEMALE

linical sign	Group Name	Admini	stration W	eek-day	· ·										
		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	
						•									
OLORED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
	640 ppm	0	0	0	3	3	3	4	4	5	5	5	5	5	
	1600 ppm	7	5	5	5	5	- 5	6	6	7	7	7	9	10	
	4000 ppm	5	3	4	6	8	8	10	10	10	10	10	10	10	
	7000 ppm	4	9	9	.9	10	10	10	10	10	10	10	10	10	
	10000 ppm	4	8	10	10	10	10	10	10	10	10	10	10	10	
ELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
	640 ppm	10	10	10	01	10	01	10	10	10	10	10	10	10	
,	1600 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10	
	4000 թթա	10	10	10	10	10	10	10	10	10	10	10	10	10	
	7000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10	
	10000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10	
MALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7000 ppm	10	0	0	0	0	0	0	0	0	0	0	0	Ò	
	10000 ppm	10	0	0	0	0	0	0	0	0	0	0.	0	0	
LIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	4000 ppm	0	0	0	0	0	0	0	0	0.	0	0	0	0	
	7000 ppm	10	0	0	. 0	0	0	0	0	0	0	0	0	0	
	10000 ppm	10	0	0	0	0	0	0	0	0	0	0	0	0	
ON REMARKABLE	Control	10	10	10	10	10	10	10	10	10	10	10	10	10	
	640 ppm	0	0	0	0	0	0	0	0	0	.0	0	0	0	
	1600 ppm	0	. 0	0	0	0	0	0	0	0	0	0	0	0	
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	

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TABLE C 1

BODY WEIGHT CHANGES AND

SURVIVAL ANIMAL NUMBERS: MALE

MEAN BODY WEIGHTS AND SURVIVAL

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STUDY NO. : 0745 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] UNIT : g REPORT TYPE : A1 13 SEX : MALE

	Control		640 p	pm		1600	ppm		4000	րրա		7000	ppm		10000	թիա	
Veek-Day ∋n Study	Av. Wt.	No.of Surviv. <10>	Av. Wt.	% of cont. <10>	No.of Surviv.	Λv. Wt.	% of cont. <10>	No.of Surviv.	Λv. ₩t.	% of cont. <10>	No.of Surviv.	Λv. Wt.	% of cont. <10>	No.of Surviv.	Λv. ₩t.	% of cont. <10>	No. of Surviv.
0-0	118 (10) 10/10	118 (10)	100	10/10	118 (10)	100	10/10	118 (10)	100	10/10	118 (10)	100	10/10	118 (10)	100	10/10
1-7	148 (10) 10/10	148 (10)	100	10/10	148 (10)	100	10/10	145 (10)	98	10/10	142 (10)	96	10/10	133 (10)	90	10/10
2-7	182 (10) 10/10	181 (10)	99	10/10	181 (10)	99	10/10	174 (10)	96	10/10	173 (10)	95	10/10	161 (10)	88	10/10
3-7	209 (10) 10/10	210 (10)	100	10/10	207 (10)	99	10/10	204 (10)	98	10/10	197 (10)	94	10/10	186 (10)	89	10/10
4-7	232 (10) 10/10	233 (10)	100	10/10	228 (10)	98	10/10	225 (10)	97	10/10	216 (10)	93	10/10	204 (10)	88	10/10
5-7	249 (10) 10/10	250 (10)	100	10/10	246 (10)	99	10/10	244 (10)	98	10/10	232 (10)	93	10/10	221 (10)	89	10/10
6-7	264 (10) 10/10	263 (10)	100	10/10	260 (10)	98	10/10	258 (10)	98	10/10	243 (10)	92	10/10	232 (10)	88	10/10
7-7	279 (10) 10/10	276 (10)	99	10/10	276 (10)	99	10/10	270 (10)	97	10/10	254 (10)	91	10/10	242 (10)	87	10/10
8-7	291 (10) 10/10	288 (10)	99	10/10	288 (10)	99	10/10	282 (10)	97	10/10	264 (10)	91	10/10	250 (10)	86	10/10
9-7	301 (10) 10/10	298 (10)	99	10/10	299 (10)	99	10/10	293 (10)	97	10/10	274 (10)	91	10/10	258 (10)	86	10/10
10-7	309 (10) 10/10	307 (10)	99	10/10	308 (10)	100	10/10	301 (10)	97	10/10	281 (10)	91	10/10	267 (10)	86	10/10
11-7	316 (10) 10/10	314 (10)	99	10/10	316 (10)	100	10/10	308 (10)	97	10/10	287 (10)	91	10/10	270 (10)	85	10/10
12-7	324 (10) 10/10	320 (10)	99	10/10	324 (10)	100	10/10	316 (10)	98	10/10	292 (10)	90	10/10	276 (10)	85	10/10
13-7	328 (10) 10/10	325 (10)	99	10/10	329 (10)	100	10/10	320 (10)	98	10/10	297 (10)	91	10/10	279 (10)	85	10/10

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TABLE C 2

### BODY WEIGHT CHANGES AND

### SURVIVAL ANIMAL NUMBERS: FEMALE

#### MEAN BODY WEIGHTS AND SURVIVAL

Av. Wt.∶g

#### STUDY NO. : 0745 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] UNIT : g REPORT TYPE : A1 13

SEX : FEMALE

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|                      | .Control |                       |     | 640 p    | pm                    |                  | 1600     | ppm                   |                  | 4000     | ինա                   |                  | 7000     | ppm                   |                  | 10000    | ppm                   |                  |
|----------------------|----------|-----------------------|-----|----------|-----------------------|------------------|----------|-----------------------|------------------|----------|-----------------------|------------------|----------|-----------------------|------------------|----------|-----------------------|------------------|
| Veek-Day<br>on Study | Av. Wt.  | No. (<br>Surv<br><10> |     | Λv.Wt.   | % of<br>cont.<br><10> | No.of<br>Surviv. | Av. Wt.  | % of<br>cont.<br><10> | No.of<br>Surviv. | Av.Wt.   | % of<br>cont.<br><10> | No.of<br>Surviv. | Av. Wt.  | % of<br>cont.<br><10> | No.of<br>Surviv. | Av. Wt.  | % of<br>cont.<br><10> | No.of<br>Surviv. |
| 0-0                  | 96 (10   | ) 10,                 | /10 | 96 (10)  | 100                   | 10/10            | 96 (10)  | 100                   | 10/10            | 96 (10)  | 100                   | 10/10            | 96 (10)  | 100                   | 10/10            | 96 (10)  | 100                   | 10/10            |
| 1-7                  | 113 (10  | ) 10,                 | /10 | 112 (10) | 99                    | 10/10            | 113 (10) | 100                   | 10/10            | 108 (10) | 96                    | 10/10            | 105 (10) | 93                    | 10/10            | 102 (10) | 90                    | 10/10            |
| 2-7                  | 127 (10  | ) 10,                 | /10 | 125 (10) | 98                    | 10/10            | 124 (10) | 98                    | 10/10            | 121 (10) | 95                    | 10/10            | 119 (10) | 94                    | 10/10            | 116 (10) | 91                    | 10/10            |
| 3-7                  | 137 (10  | ) 10,                 | /10 | 138 (10) | 101                   | 10/10            | 137 (10) | 100                   | 10/10            | 131 (10) | 96                    | 10/10            | 128 (10) | 93                    | 10/10            | 125 (10) | 91                    | 10/10            |
| 4-7                  | 145 (10  | ) 10,                 | /10 | 146 (10) | 101                   | 10/10            | 144 (10) | 99                    | 10/10            | 137 (10) | 94                    | 10/10            | 135 (10) | 93                    | 10/10            | 131 (10) | 90                    | 10/10            |
| 5-7                  | 154 (10  | ) 10,                 | /10 | 155 (10) | 101                   | 10/10            | 151 (10) | 98                    | 10/10            | 142 (10) | 92                    | 10/10            | 141 (10) | 92                    | 10/10            | 136 (10) | 88                    | 10/10            |
| 6-7                  | 159 (10  | ) 10,                 | /10 | 161 (10) | 101                   | 10/10            | 157 (10) | 99                    | 10/10            | 149 (10) | 94                    | 10/10            | 146 (10) | 92                    | 10/10            | 141 (10) | 89                    | 10/10            |
| 7-7                  | 168 (10  | ) 10,                 | /10 | 168 (10) | 100                   | 10/10            | 161 (10) | 96                    | 10/10            | 154 (10) | 92                    | 10/10            | 151 (10) | 90                    | 10/10            | 146 (10) | 87                    | 10/10            |
| 8-7                  | 172 (10  | ) 10,                 | /10 | 170 (10) | 99                    | 10/10            | 165 (10) | 96                    | 10/10            | 158 (10) | 92                    | 10/10            | 154 (10) | 90                    | 10/10            | 149 (10) | 87                    | 10/10            |
| 9-7                  | 177 (10  | ) 10,                 | /10 | 175 (10) | 99                    | 10/10            | 169 (10) | 95                    | 10/10            | 161 (10) | 91                    | 10/10            | 158 (10) | 89                    | 10/10            | 152 (10) | 86                    | 10/10            |
| 10-7                 | 180 (10  | ) 10,                 | /10 | 178 (10) | 99                    | 10/10            | 173 (10) | 96                    | 10/10            | 165 (10) | 92                    | 10/10            | 160 (10) | 89                    | 10/10            | 155 (10) | 86                    | 10/10            |
| 11-7                 | 184 (10  | )) 10,                | /10 | 182 (10) | 99                    | 10/10            | 177 (10) | 96                    | 10/10            | 167 (10) | 91                    | 10/10            | 162 (10) | 88                    | 10/10            | 158 (10) | 86                    | 10/10            |
| 12-7                 | 186 (10  | ) 10,                 | /10 | 184 (10) | 99                    | 10/10            | 178 (10) | 96                    | 10/10            | 168 (10) | 90                    | 10/10            | 165 (10) | 89                    | 10/10            | 160 (10) | 86                    | 10/10            |
| 13-7                 | 188 (10  | ) 10,                 | /10 | 186 (10) | 99                    | 10/10            | 180 (10) | 96                    | 10/10            | 171 (10) | 91                    | 10/10            | 166 (10) | 88                    | 10/10            | 163 (10) | 87                    | 10/10            |

< >:No. of effective animals, ( ):No. of measured animals

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TABLE C 3

### BODY WEIGHT CHANGES: MALE

|      |                              | Week-day                                                                    |                                                                                                   |                                                                                                                            |                                                                                                                                            |                                                                                                                                                    |                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                            |
|------|------------------------------|-----------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 0-0  |                              | I-7                                                                         |                                                                                                   | 2-7                                                                                                                        |                                                                                                                                            | 3-7                                                                                                                                                |                                                                                                                                                                                                                                                                                    | 47                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                   | 5-7                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                | 6-7                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                            |
| 118土 | 3                            | 148土                                                                        | 3                                                                                                 | $182\pm$                                                                                                                   | 5                                                                                                                                          | $209\pm$                                                                                                                                           | 4 .                                                                                                                                                                                                                                                                                | 232±                                                                                                                                                                                                                                                                                                                  | 4                                                                                                                                                                                                                                                                                                                                                                 | 249土                                                                                                                                                                                                                                                                                                                                                                                                 | 5                                                                                                                                                                                                                                                                                                              | 264-1-                                                                                                                                                                                                                                                                                                         | 6                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                            |
| 118± | 4                            | $148\pm$                                                                    | 7                                                                                                 | 181±                                                                                                                       | 7                                                                                                                                          | 210±                                                                                                                                               | 7                                                                                                                                                                                                                                                                                  | 233±                                                                                                                                                                                                                                                                                                                  | 8                                                                                                                                                                                                                                                                                                                                                                 | 250±                                                                                                                                                                                                                                                                                                                                                                                                 | 9                                                                                                                                                                                                                                                                                                              | 263±                                                                                                                                                                                                                                                                                                           | 11                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                            |
| 118± | 3                            | 148±                                                                        | 5                                                                                                 | 181±                                                                                                                       | 6                                                                                                                                          | $207\pm$                                                                                                                                           | 8                                                                                                                                                                                                                                                                                  | 228±                                                                                                                                                                                                                                                                                                                  | 9                                                                                                                                                                                                                                                                                                                                                                 | 246±                                                                                                                                                                                                                                                                                                                                                                                                 | 9                                                                                                                                                                                                                                                                                                              | $260\pm$                                                                                                                                                                                                                                                                                                       | 12                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                            |
| 118± | 4                            | 145±                                                                        | 7                                                                                                 | 174±                                                                                                                       | 11                                                                                                                                         | 204±                                                                                                                                               | 10                                                                                                                                                                                                                                                                                 | $225\pm$                                                                                                                                                                                                                                                                                                              | 12                                                                                                                                                                                                                                                                                                                                                                | $244\pm$                                                                                                                                                                                                                                                                                                                                                                                             | 12                                                                                                                                                                                                                                                                                                             | $258\pm$                                                                                                                                                                                                                                                                                                       | 13                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                            |
| 118土 | 4                            | 142±                                                                        | 5*                                                                                                | 173±                                                                                                                       | 6*                                                                                                                                         | 197土                                                                                                                                               | 6**                                                                                                                                                                                                                                                                                | 216±                                                                                                                                                                                                                                                                                                                  | 6**                                                                                                                                                                                                                                                                                                                                                               | <b>2</b> 32±                                                                                                                                                                                                                                                                                                                                                                                         | 8**                                                                                                                                                                                                                                                                                                            | $243\pm$                                                                                                                                                                                                                                                                                                       | 8**                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                            |
| 118± | 4                            | $133\pm$                                                                    | 5**                                                                                               | 161±                                                                                                                       | 7 <b>*</b> *                                                                                                                               | 186±                                                                                                                                               | 8**                                                                                                                                                                                                                                                                                | 204±                                                                                                                                                                                                                                                                                                                  | 10**                                                                                                                                                                                                                                                                                                                                                              | 221±                                                                                                                                                                                                                                                                                                                                                                                                 | 10**                                                                                                                                                                                                                                                                                                           | $232\pm$                                                                                                                                                                                                                                                                                                       | 10**                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                            |
|      |                              |                                                                             |                                                                                                   |                                                                                                                            |                                                                                                                                            |                                                                                                                                                    |                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                            |
|      | 118±<br>118±<br>118±<br>118± | 118±       4         118±       3         118±       4         118±       4 | 118±     4     148±       118±     3     148±       118±     4     145±       118±     4     142± | 118±     4     148±     7       118±     3     148±     5       118±     4     145±     7       118±     4     142±     5* | $118 \pm$ 4 $148 \pm$ 7 $181 \pm$ $118 \pm$ 3 $148 \pm$ 5 $181 \pm$ $118 \pm$ 4 $145 \pm$ 7 $174 \pm$ $118 \pm$ 4 $142 \pm$ $5*$ $173 \pm$ | $118 \pm$ 4 $148 \pm$ 7 $181 \pm$ 7 $118 \pm$ 3 $148 \pm$ 5 $181 \pm$ 6 $118 \pm$ 4 $145 \pm$ 7 $174 \pm$ 11 $118 \pm$ 4 $142 \pm$ 5* $173 \pm$ 6* | 118±       4       148±       7       181±       7       210±         118±       3       148±       5       181±       6       207±         118±       4       145±       7       174±       11       204±         118±       4       142±       5*       173±       6*       197± | 118±       4       148±       7       181±       7       210±       7         118±       3       148±       5       181±       6       207±       8         118±       4       145±       7       174±       11       204±       10         118±       4       142±       5*       173±       6*       197±       6** | 118±       4       148±       7       181±       7       210±       7       233±         118±       3       148±       5       181±       6       207±       8       228±         118±       4       145±       7       174±       11       204±       10       225±         118±       4       142±       5*       173±       6*       197±       6**       216± | 118±       4       148±       7       181±       7       210±       7       233±       8         118±       3       148±       5       181±       6       207±       8       228±       9         118±       4       145±       7       174±       11       204±       10       225±       12         118±       4       142±       5*       173±       6*       197±       6**       216±       6** | $118 \pm$ 4 $148 \pm$ 7 $181 \pm$ 7 $210 \pm$ 7 $233 \pm$ 8 $250 \pm$ $118 \pm$ 3 $148 \pm$ 5 $181 \pm$ 6 $207 \pm$ 8 $228 \pm$ 9 $246 \pm$ $118 \pm$ 4 $145 \pm$ 7 $174 \pm$ $11$ $204 \pm$ $10$ $225 \pm$ $12$ $244 \pm$ $118 \pm$ 4 $142 \pm$ $5*$ $173 \pm$ $6*$ $197 \pm$ $6**$ $216 \pm$ $6**$ $232 \pm$ | $118 \pm$ 4 $148 \pm$ 7 $181 \pm$ 7 $210 \pm$ 7 $233 \pm$ 8 $250 \pm$ 9 $118 \pm$ 3 $148 \pm$ 5 $181 \pm$ 6 $207 \pm$ 8 $228 \pm$ 9 $246 \pm$ 9 $118 \pm$ 4 $145 \pm$ 7 $174 \pm$ 11 $204 \pm$ 10 $225 \pm$ 12 $244 \pm$ 12 $118 \pm$ 4 $142 \pm$ 5* $173 \pm$ 6* $197 \pm$ 6*** $216 \pm$ 6*** $232 \pm$ 8*** | $118 \pm$ 4 $148 \pm$ 7 $181 \pm$ 7 $210 \pm$ 7 $233 \pm$ 8 $250 \pm$ 9 $263 \pm$ $118 \pm$ 3 $148 \pm$ 5 $181 \pm$ 6 $207 \pm$ 8 $228 \pm$ 9 $246 \pm$ 9 $260 \pm$ $118 \pm$ 4 $145 \pm$ 7 $174 \pm$ 11 $204 \pm$ 10 $225 \pm$ 12 $244 \pm$ 12 $258 \pm$ $118 \pm$ 4 $142 \pm$ 5* $173 \pm$ 6* $197 \pm$ 6** $216 \pm$ 6** $232 \pm$ 8** $243 \pm$ | $118 \pm$ 4 $148 \pm$ 7 $181 \pm$ 7 $210 \pm$ 7 $233 \pm$ 8 $250 \pm$ 9 $263 \pm$ 11 $118 \pm$ 3 $148 \pm$ 5 $181 \pm$ 6 $207 \pm$ 8 $228 \pm$ 9 $246 \pm$ 9 $260 \pm$ 12 $118 \pm$ 4 $145 \pm$ 7 $174 \pm$ 11 $204 \pm$ 10 $225 \pm$ 12 $244 \pm$ 12 $258 \pm$ 13 $118 \pm$ 4 $142 \pm$ 5* $173 \pm$ $6*$ $197 \pm$ $6**$ $216 \pm$ $6**$ $232 \pm$ $8**$ $243 \pm$ $8**$ |

(SUMMARY)

BODY WEIGHT CHANGES

STUDY NO. : 0745

UNIT : g REPORT TYPE : A1 13 PAGE : 2 SEX : MALE Administration week-day\_ Group Name 12-7 13-7 8-7 9-7 10-7 11-7 7-7  $316 \pm 8$ 324土 9  $328\pm$ 8 Control 279 土 7 291土 8  $301\pm$  8  $309 \pm 9$ 640 ppm 276± 11 288± 14 298± 13 307± 13 314± 13 320± 11 325± 11 316± 12 324土 13 329± 14 1600 ppm 276± 11 288± 11 299± 12  $308 \pm 12$ 4000 ppm 270± 16 282± 17 293± 19  $301\pm$  20 308± 21 316± 22 320± 22 7000 ppm  $254\pm$ 8\*\*  $264\pm$ 8\*\*  $274\pm$ 9\*\*  $281\pm$ 9\*\*  $287\pm$ 7\*\*  $292\pm$ 8\*\* 297 土 8\*\* 270± 11\*\* 276± 12\*\* 279± 10\*\* 10000 ppm 242± 11\*\* 250± 11\*\* 258± 12\*\* 267± 11\*\* Test of Dunnett Significant difference ; \* : P  $\leq$  0.05 \*\* : P ≦ 0.01 (HAN260) BAIS 4

(SUMMARY)

BODY WEIGHT CHANGES

ALL ANIMALS

STUDY NO. : 0745

ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]

 $\sim 2$ 

TABLE C 4

### BODY WEIGHT CHANGES: FEMALE

| Group Name | Admini<br>0-0 | stration | week-day<br>1-7 |     | 2–7      |             | 3-7  |     | 4-7  |     | 5-7           |     | 6-7      |     |
|------------|---------------|----------|-----------------|-----|----------|-------------|------|-----|------|-----|---------------|-----|----------|-----|
| Control    | 96±           | 2        | 113±            | 3   | 127±     | 2           | 137土 | 4   | 145土 | 5   | $154\pm$      | 7   | 159±     | 7   |
| 640 ppm    | 96±           | 2        | 112±            | 4   | $125\pm$ | 5           | 138± | 6   | 146± | 8   | 155±          | 8   | $161\pm$ | 9   |
| 1600 ppm   | 96土           | 2        | 113±            | 4   | 124生     | 5           | 137± | 4   | 144± | 5   | 151±          | 6   | 157±     | 7   |
| 4000 ppm   | $96\pm$       | 2        | 108土            | 3*  | 121±     | 3**         | 131± | 4** | 137± | 3** | 1 <b>42</b> ± | 4** | 149土     | 3** |
| 7000 ppm   | 96±           | 2        | 105土            | 3** | 119±     | 4 <b>**</b> | 128土 | 4** | 135土 | 4** | 141土          | 3** | 146 ±    | 4** |
| 10000 ppm  | 96±           | 2        | 102±            | 3** | $116\pm$ | 3**         | 125± | 3** | 131± | 3** | 136±          | 4** | 141土     | 4** |

BODY WEIGHT CHANGES STUDY NO. : 0745 ALL ANIMALS ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] UNIT : g REPORT TYPE : A1 13 SEX : FEMALE

PAGE : 4

| roup Name                             | Administ  | tration | week-day      |     |      |              |           |       |      |              |               |     |       |     |
|---------------------------------------|-----------|---------|---------------|-----|------|--------------|-----------|-------|------|--------------|---------------|-----|-------|-----|
| -                                     | 7–7       |         | 8-7           |     | 9-7  |              | 107       |       | 11-7 |              | 12-7          |     | 13-7  |     |
| ontrol                                | 168土      | 8       | 172土          | 8   | 177± | 10           | 180 ±     | 10    | 184土 | 9            | 186土          | 10  | 188土  | 9   |
| 40 ppm                                | 168± 1    | 10      | 170±          | 10  | 175± | 10           | 178±      | 10    | 182± | 11           | 1 <b>84</b> ± | 11  | 186±  | 10  |
| 600 ppm                               | 161±      | 8       | 165±          | 8   | 169± | 9            | 173±      | 10    | 177± | 10           | 178±          | 11  | 180±  | 11  |
| 1000 ppm                              | 154±      | 5**     | 158±          | 6** | 161土 | 6**          | $165\pm$  | 7**   | 167± | 8**          | 168±          | 7** | 171±  | 8** |
| 000 ppm                               | 151土      | 3**     | 154 <u>-ŀ</u> | 4** | 158± | 5**          | $160\pm$  | . 5** | 162土 | 5 <b>*</b> * | 165土          | 4** | 166 ± | 6** |
| LOOOO ppm                             | $146\pm$  | 5**     | 149±          | 4** | 152± | 4 <b>*</b> * | $155\pm$  | 5**   | 158± | 5**          | $160\pm$      | 5** | 163±  | 6** |
| · · · · · · · · · · · · · · · · · · · |           |         |               |     |      |              |           |       |      |              |               |     |       |     |
| Significant difference ;              | *:P ≦ 0.0 | 05 *    | * : P ≦ 0.0   | L   |      |              | Test of D | umett |      |              |               |     |       |     |
| (HAN260)                              |           |         |               |     |      |              |           |       |      |              |               |     |       |     |

(SUMMARY)

#### TABLE D 1

### FOOD CONSUMPTION CHANGES AND

### SURVIVAL ANIMAL NUMBERS: MALE

#### MEAN FOOD CONSUMPTION (FC) AND SURVIVAL

#### STUDY NO. : 0745 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] UNIT : g REPORT TYPE : A1 13

SEX : MALE

|                      | Control  |                          | 640 p     | nu (                  |                  | 1600      | ppm                   |                  | 4000      | իրա                   |                   | 7000      | ppm                   |                  | 10000     | նիա                   |                  |
|----------------------|----------|--------------------------|-----------|-----------------------|------------------|-----------|-----------------------|------------------|-----------|-----------------------|-------------------|-----------|-----------------------|------------------|-----------|-----------------------|------------------|
| Veek-Day<br>on Study | Λν. FC.  | No.of<br>Surviv.<br><10> | Av. FC.   | % of<br>cont.<br><10> | No.of<br>Surviv. | Av. FC.   | % of<br>cont.<br><10> | No.of<br>Surviv. | Av. FC.   | % of<br>cont.<br><10> | No. of<br>Surviv. | Av. FC.   | % of<br>cont.<br><10> | No.of<br>Surviv. | Av. FC.   | % of<br>cont.<br><10> | No.of<br>Surviv. |
| 1-7                  | 13.2 (1  | ) 10/10                  | 13.0 (10) | - 98                  | 10/10            | 13.0 (10) | 98                    | 10/10            | 12.2 (10) | 92                    | 10/10             | 11.1 (10) | 84                    | 10/10            | 9.4 (10)  | 71                    | 10/10            |
| 2-7                  | 14.4 (10 | ) 10/10                  | 14.4 (10) | 100                   | 10/10            | 14.5 (10) | 101                   | 10/10            | 13.6 (10) | 94                    | 10/10             | 13.2 (10) | 92                    | 10/10            | 12.6 (10) | 88                    | 10/10            |
| 3-7                  | 15.0 (1  | ) 10/10                  | 15.3 (10) | 102                   | 10/10            | 14.8 (10) | 99                    | 10/10            | 14.7 (10) | 98.                   | 10/10             | 13.7 (10) | 91                    | 10/10            | 13.2 (10) | 88                    | 10/10            |
| 4-7                  | 15.2 (10 | ) 10/10                  | 15.4 (10) | 101                   | 10/10            | 15.0 (10) | 99                    | 10/10            | 14.9 (10) | 98                    | 10/10             | 13.6 (10) | 89                    | 10/10            | 13.1 (10) | 86                    | 10/10            |
| 5-7                  | 15.2 (1  | ) 10/10                  | 15.2 (10) | 100                   | 10/10            | 14.9 (10) | 98                    | 10/10            | 14.9 (10) | 98                    | 10/10             | 13.6 (10) | 89                    | 10/10            | 13.4 (10) | 88                    | 10/10            |
| 6-7                  | 15.1 (10 | ) 10/10                  | 15.0 (10) | 99                    | 10/10            | 14.6 (10) | 97                    | 10/10            | 14.6 (10) | 97                    | 10/10             | 13.4 (10) | 89                    | 10/10            | 13.0 (10) | 86                    | 10/10            |
| 7-7                  | 15.5 (1) | ) 10/10                  | 15.5 (10) | 100                   | 10/10            | 15.1 (10) | 97                    | 10/10            | 14.9 (10) | 96                    | 10/10             | 13.5 (10) | 87                    | 10/10            | 13.1 (10) | 85                    | 10/10            |
| 8-7                  | 15.4 (1) | ) 10/10                  | 15.4 (10) | 100                   | 10/10            | 15.0 (10) | 97                    | 10/10            | 14.7 (10) | 95                    | 10/10             | 13.2 (10) | 86                    | 10/10            | 12.7 (10) | 82                    | 10/10            |
| 9-7                  | 15.4 (1) | ) 10/10                  | 15.6 (10) | 101                   | 10/10            | 15.2 (10) | 99                    | 10/10            | 15.0 (10) | 97                    | 10/10             | 13.6 (10) | 88                    | 10/10            | 13.1 (10) | 85                    | 10/10            |
| 10-7                 | 15.1 (1) | ) 10/10                  | 15.4 (10) | 102                   | 10/10            | 15.0 (10) | 99                    | 10/10            | 14.7 (10) | 97                    | 10/10             | 13.5 (10) | 89                    | 10/10            | 13.0 (10) | 86                    | 10/10            |
| 11-7                 | 14.9 (10 | ) 10/10                  | 15.0 (10) | 101                   | 10/10            | 14.6 (10) | 98                    | 10/10            | 14.5 (10) | 97                    | 10/10             | 13.3 (10) | 89                    | 10/10            | 12.5 (10) | 84                    | 10/10            |
| 12-7                 | 14.9 (1  | ) 10/10                  | 14.8 (10) | 99                    | 10/10            | 14.7 (10) | 99                    | 10/10            | 14.4 (10) | 97                    | 10/10             | 13.3 (10) | 89                    | 10/10            | 12.7 (10) | 85                    | 10/10            |
| 13-7                 | 14.8 (1  | ) 10/10                  | 14.7 (10) | 99                    | 10/10            | 14.4 (10) | 97                    | 10/10            | 14.5 (10) | 98                    | 10/10             | 13.3 (10) | 90                    | 10/10            | 12.5 (10) | 84                    | 10/10            |

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TABLE D 2

## FOOD CONSUMPTION CHANGES AND

### SURVIVAL ANIMAL NUMBERS: FEMALE

#### MEAN FOOD CONSUMPTION (FC) AND SURVIVAL

#### STUDY NO. : 0745 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] : g UNIT REPORT TYPE : A1 13 : FEMALE SEX .

|                      | Control  |                          | 640 µ     | ipm                   |                  | 1600      | րիա                   |                  | 4000      | ինա                   |                  | 7000     | ppm                   |                  | 10000    | ppm                   |                   |
|----------------------|----------|--------------------------|-----------|-----------------------|------------------|-----------|-----------------------|------------------|-----------|-----------------------|------------------|----------|-----------------------|------------------|----------|-----------------------|-------------------|
| Week-Day<br>on Study | Av. FC.  | No.of<br>Surviv.<br><10> | Av. FC.   | % of<br>cont.<br><10> | No.of<br>Surviv. | Av. FC.   | % of<br>cont.<br><10> | No.of<br>Surviv. | Λv. FC.   | % of<br>cont.<br><10> | No.of<br>Surviv. | Av. FC.  | % of<br>cont.<br><10> | No.of<br>Surviv. | Λv. FC.  | % of<br>cont.<br><10> | No. of<br>Surviv. |
| 1-7                  | 10.8 (10 | ) 10/10                  | 10.3 (10) | 95                    | 10/10            | 10.1 (10) | 94                    | 10/10            | 9.4 (10)  | 87                    | 10/10            | 8.2 (10) | 76                    | 10/10            | 7.5 (10) | 69                    | 10/10             |
| 2-7                  | 10.8 (10 | ) 10/10                  | 10.5 (10) | 97                    | 10/10            | 10.5 (10) | 97                    | 10/10            | 10.1 (10) | 94                    | 10/10            | 9.6 (10) | 89                    | 10/10            | 9.6 (10) | 89                    | 10/10             |
| 3-7                  | 10.9 (10 | ) 10/10                  | 10.9 (10) | 100                   | 10/10            | 10.5 (10) | 96                    | 10/10            | 10.3 (10) | 94                    | 10/10            | 9.4 (10) | 86                    | 10/10            | 9.3 (10) | 85                    | 10/10             |
| 4-7                  | 10.8 (10 | ) 10/10                  | 10.9 (10) | 101                   | 10/10            | 10.5 (10) | 97                    | 10/10            | 10.3 (10) | 95                    | 10/10            | 9.3 (10) | 86                    | 10/10            | 8.9 (10) | 82                    | 10/10             |
| 5-7                  | 11.0 (10 | ) 10/10                  | 11.1 (10) | 101                   | 10/10            | 10.5 (10) | 95                    | 10/10            | 10.4 (10) | 95                    | 10/10            | 9.5 (10) | 86                    | 10/10            | 8.8 (10) | 80                    | 10/10             |
| 6-7                  | 11.0 (10 | ) 10/10                  | 10.9 (10) | 99                    | 10/10            | 10.0 (10) | 91                    | 10/10            | 10.1 (10) | 92                    | 10/10            | 9.3 (10) | 85                    | 10/10            | 8.7 (10) | 79                    | 10/10             |
| 7-7                  | 11.3 (10 | ) 10/10                  | 11.1 (10) | 98                    | 10/10            | 10.2 (10) | 90                    | 10/10            | 10.5 (10) | 93                    | 10/10            | 9.1 (9)  | 81                    | 10/10            | 8.8 (10) | 78                    | 10/10             |
| 8-7                  | 11.0 (10 | ) 10/10                  | 10.4 (10) | 95                    | 10/10            | 9.7 (10)  | 88                    | 10/10            | 10.0 (10) | 91                    | 10/10            | 9.1 (10) | 83                    | 10/10            | 8.4 (10) | 76                    | 10/10             |
| 9-7                  | 11.2 (10 | ) 10/10                  | 10.7 (10) | 96                    | 10/10            | 9.9 (10)  | 88                    | 10/10            | 10.0 (10) | 89                    | 10/10            | 9.1 (10) | 81                    | 10/10            | 8.5 (10) | 76                    | 10/10             |
| 10-7                 | 10.8 (10 | ) 10/10                  | 10.6 (10) | 98                    | 10/10            | 9.9 (10)  | 92                    | 10/10            | 10.0 (10) | 93                    | 10/10            | 9.0 (10) | 83                    | 10/10            | 8.5 (10) | 79                    | 10/10             |
| 11-7                 | 10.8 (10 | ) 10/10                  | 10.4 (10) | 96                    | 10/10            | 9.7 (10)  | 90                    | 10/10            | 9.9 (10)  | 92                    | 10/10            | 8.8 (10) | 81                    | 10/10            | 8.4 (10) | 78                    | 10/10             |
| 12-7                 | 10.7 (10 | ) 10/10                  | 10.3 (10) | 96                    | 10/10            | 9.9 (10)  | 93                    | 10/10            | 9.8 (10)  | 92                    | 10/10            | 9.0 (10) | 84                    | 10/10            | 8.4 (10) | 79                    | 10/10             |
| 13-7                 | 10.5 (10 | ) 10/10                  | 10.2 (10) | 97                    | 10/10            | 9.6 (10)  | 91                    | 10/10            | 9.9 (10)  | 94                    | 10/10            | 8.9 (10) | 85                    | 10/10            | 8.5 (10) | 81                    | 10/10             |

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TABLE D 3

### FOOD CONSUMPTION CHANGES: MALE

STUDY NO. : 0745 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] UNIT : g REPORT TYPE : A1 13 SEX : MALE

#### FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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| Group Name | Administration 1-7(7) | veek-day(effective)<br>2-7(7) | 3-7(7)      | 4-7(7)       | 5-7(7)      | 6-7(7)         | 7-7(7)      |  |
|------------|-----------------------|-------------------------------|-------------|--------------|-------------|----------------|-------------|--|
|            |                       |                               |             |              |             |                |             |  |
| Control    | $13.2\pm$ 0.7         | 14.4土 0.6                     | 15.0± 0.6   | 15. 2 土 0. 5 | 15.2± 0.7   | 15.1 ± 0.7     | 15.5± 0.8   |  |
| 640 ppm    | 13.0± 0.6             | 14.4± 0.8                     | 15.3± 0.6   | 15.4± 0.6    | 15.2± 0.5   | 15.0± 0.9      | 15.5± 1.0   |  |
| 1600 ppm   | 13.0± 0.5             | 14.5± 0.6                     | 14.8± 0.6   | 15.0± 0.5    | 14.9± 0.5   | 14.6 ± 0.5     | 15.1± 0.6   |  |
| 4000 թեու  | 12.2± 0.9**           | 13.6± 1.1*                    | 14.7± 0.8   | 14.9± 0.9    | 14.9± 0.9   | 14.6± 0.7      | [4.9± 1.0   |  |
| 7000 ppm   | 11.1土 0.5**           | 13.2± 0.6**                   | 13.7± 0.6** | 13.6土 0.7**  | 13.6± 0.6** | 13. 4 - 0. 6** | 13.5土 0.6** |  |
| 10000 ppm  | 9.4± 0.7**            | 12.6± 0.5**                   | 13.2± 0.7** | 13.1± 0.7**  | 13.4± 0.6** | 13.0± 0.7**    | 13.1± 0.8** |  |

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

Test of Dunnett

(HAN260)

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STUDY NO. : 0745 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] UNIT : g REPORT TYPE : A1 13 SEX : MALE

#### FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE : 2

| Group Name           | Administration<br>8-7(7) | week-day(effective)<br>9-7(7) | 10-7 (7)    | 11-7 (7)        | 12-7(7)     | 13-7 (7)             |      |
|----------------------|--------------------------|-------------------------------|-------------|-----------------|-------------|----------------------|------|
|                      |                          | 15 4.4 0 7                    | 15.1± 0.6   | 14.9± 0.7       | 14.9± 0.8   | 14.8土 0.6            |      |
| ontrol               | 15.4 生 0.7               | 15.4 ± 0.7                    | 13.1 0.6    | 14.9 - 0.7      | 14.9 - 0.0  | 14.61 0.0            |      |
| 640 ppm              | 15.4± 0.8                | 15.6± 0.9                     | 15.4± 0.8   | $15.0\pm0.8$    | 14.8± 0.8   | 14.7 $\pm$ 0.7       |      |
| 600 ppm              | 15.0± 0.5                | 15.2± 0.6                     | 15.0± 0.5   | 14.6± 0.5       | 14.7± 0.6   | 14.4± 0.6            |      |
| 000 ppm              | 14.7± 1.0                | 15.0± 1.1                     | 14.7± 1.0   | 14.5± 1.2       | 14.4± 0.9   | 14.5± 1.0            |      |
| 000 ppm              | 13.2± 0.4**              | 13.6土 0.5**                   | 13.5± 0.5** | 13.3± 0.4**     | 13.3± 0.6** | 13.3± 0.5 <b>≭</b> ∗ |      |
| 0000 ppm             | 12.7± 0.8**              | 13.1± 0.8**                   | 13.0± 0.8** | 12.5± 0.7**     | 12.7± 0.6₩  | 12.5± 0.5**          |      |
|                      |                          |                               |             |                 |             |                      |      |
| Significant differen | nce; $*: P \leq 0.05$ *  | ** : P ≦ 0.01                 |             | Test of Dunnett |             |                      |      |
| HAN260)              |                          |                               |             |                 |             |                      | BAIS |

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TABLE D 4

### FOOD CONSUMPTION CHANGES: FEMALE

STUDY NO. : 0745 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] UNIT : g REPORT TYPE : A1 13 SEX : FEMALE

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FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE : 3

| Group Name         |                          | week-day(effective) |            |                 |                |                             |                     |  |
|--------------------|--------------------------|---------------------|------------|-----------------|----------------|-----------------------------|---------------------|--|
|                    | 1-7(7)                   | 2-7(7)              | 3-7(7)     | 4-7(7)          | 5-7(7)         | 6-7(7)                      | 7-7(7)              |  |
| ontrol             | 10.8± 0.3                | 10.8主 0.4           | 10.9± 0.4  | 10.8土 0.5       | 11.0± 0.8      | 11.0 <u>-+</u> 0.7          | 11.3± 0.7           |  |
| lO ppm             | 10.3± 0.4                | 10.5± 0.5           | 10.9± 0.8  | 10.9± 0.7       | 11.1± 0.8      | 10.9± 0.7                   | 11.1± 0.7           |  |
| 600 ppm            | 10.1± 0.5**              | 10.5± 0.5           | 10.5± 0.6  | 10.5± 0.7       | 10.5± 0.7      | 10.0± 0.6**                 | 10.2± 0.7**         |  |
| 000 ppm            | 9.4± 0.4≉*               | 10.1± 0.6*          | 10.3± 0.4* | 10.3± 0.4       | 10.4 $\pm$ 0.5 | 10.1± 0.5*                  | 10.5± 0.6*          |  |
| 000 ppm            | 8.2± 0.5**               | 9.6± 0.5 <b>*</b> * | 9.4± 0.4** | 9.3± 0.5**      | 9.5± 0.8≉≉     | 9.3 <u>+</u> 0.7 <b>*</b> * | 9.1± 0.3 <b>*</b> * |  |
| 10000 mgm          | 7.5± 0.3★★               | 9.6± 0.4**          | 9.3± 0.4** | 8.9± 0.5**      | 8.8± 0.4**     | 8.7± 0.4**                  | 8.8± 0.5**          |  |
|                    |                          |                     |            |                 |                |                             |                     |  |
| Significant differ | ence ; * : $P \leq 0.05$ | ** : P ≦ 0.01       |            | Test of Dunnett |                |                             |                     |  |
| (HAN260)           |                          |                     |            |                 |                |                             |                     |  |

STUDY NO. : 0745 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] UNIT : g REPORT TYPE : A1 13 SEX : FEMALE

#### FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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PAGE : 4

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| Group Name          | Administration<br>8-7(7) | week-day(effective)<br>9-7(7) | 10-7(7)    | 11-7(7)             | 12-7(7)    | 13-7 (7)   |             |
|---------------------|--------------------------|-------------------------------|------------|---------------------|------------|------------|-------------|
| Control             | 11.0± 0.9                | 11.2土 0.8                     | 10.8± 0.7  | 10.8± 0.4           | 10.7± 0.6  | 10.5土 0.6  |             |
| 640 ppm             | 10.4± 0.6                | 10.7± 0.6                     | 10.6± 0.7  | 10.4± 0.8           | 10.3± 0.9  | 10.2± 0.7  |             |
| 1600 ppm            | 9.7± 0.8**               | 9.9± 0.9**                    | 9.9± 1.0*  | 9.7± 1.1**          | 9.9± 1.0*  | 9.6± 1.0*  | -<br>-<br>- |
| 4000 ppm            | 10.0± 0.6**              | 10.0± 0.4**                   | 10.0± 0.7* | 9.9± 0.6**          | 9.8± 0.6*  | 9.9± 0.6   |             |
| 7000 ppm            | 9.1± 0.5 <b>*</b> *      | 9.1± 0.5 <b>*</b> *           | 9.0± 0.5** | 8.8± 0.4 <b>*</b> * | 9.0± 0.4** | 8.9± 0.6** |             |
| 10000 mqq           | 8.4± 0.4**               | 8.5± 0.4**                    | 8.5± 0.3** | 8.4± 0.4**          | 8.4± 0.3** | 8.5± 0.4** |             |
|                     |                          |                               |            |                     |            |            |             |
| Significant differe | nce; $*: P \leq 0.05$    | ** : P ≤ 0.01                 |            | Test of Dunnett     |            |            |             |
| (HAN260)            |                          |                               |            |                     |            |            | BAIS 4      |

TABLE E 1

### CHEMICAL INTAKE CHANGES: MALE

STUDY NO. : 0745 ANIMAL : RAT F344/DuCr1Cr1;j[F344/DuCr;j] UNIT : mg/kg/day REPORT TYPE : A1 13 SEX : MALE CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANIMALS

PAGE : 1

| Group Name | Adminis     | tration | (weeks)     |    |              |     |              |    |                     |    |                     |     |               |    |  |
|------------|-------------|---------|-------------|----|--------------|-----|--------------|----|---------------------|----|---------------------|-----|---------------|----|--|
|            | 1           |         | 2           |    | 3            |     | . 4          |    | 5                   |    | 6                   |     | 7             |    |  |
|            |             |         |             |    |              |     |              |    |                     |    |                     |     |               |    |  |
| Control    | 0 -止        | 0       | $0\pm$      | 0  | 0 <u>-1-</u> | 0   | 0±           | 0  | 0土                  | 0  | 0土                  | 0   | 0±            | 0  |  |
| C10        | 56±         |         | 51±         | 2  | <b>4</b> 6±  |     | 42±          | 1  | 39±                 | 1  | 37±                 | 1   | 36±           | 1  |  |
| 640 ppm    | 90 <u>-</u> | 1       | 51 <u>–</u> | 2  | 40 -         | 1   | 42           | ĩ  | 39 <u>-</u>         | 1  | 31 -                | 1   | 50 ±          | 1  |  |
| 1600 ppm   | 141±        | 3       | $128\pm$    | 3  | 114±         | 3   | $105\pm$     | 3  | $97\pm$             | 3  | $90\pm$             | 3   | 88±           | 2  |  |
| 4000 mu    | $336\pm$    | 13      | 311±        | 9  | 289±         | . 8 | 265±         | 8  | 245土                | 5  | 227±                | 5   | 221±          | 6  |  |
|            | 500±        | 15      | 511-        | 5  | 205 -        | . 0 | 200          | Ū  | <b>D</b> 40 <u></u> | U  | <i>501</i> <u> </u> | U U | 251-          | Ū  |  |
| 7000 ppm   | 547土        | 14      | $531\pm$    | 15 | 485±         | 14  | <b>440</b> ± | 11 | 408土                | 9  | $386\pm$            | 8   | 370土          | 11 |  |
| 10000      | 709+        | 30      | 784±        | 24 | 707±         | 25  | 642±         | 22 | 608±                | 12 | 561±                | 13  | 542±          | 16 |  |
| 10000 mqq  | 708±        | 30      | 784±        | 24 | 107±         | 20  | 042 <b>工</b> | 44 | 008 ±               | 12 | 301 ±               | 13  | 04 <i>2</i> ± | 10 |  |

(HAN300)

BAIS 4

CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANIMALS

STUDY NO. : 0745 ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj] UNIT mg/kg/day REPORT TYPE : A1 13 SEX : MALE

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PAGE : 2

| Group Name | Administration (weeks) |    |          |    |          |    |          |    |          |    |              |    | <br> |
|------------|------------------------|----|----------|----|----------|----|----------|----|----------|----|--------------|----|------|
| -          | 8                      |    | 9        |    | 10       |    | 11       |    | 12       |    | 13           |    |      |
| Control    | 0土                     | 0  | 0 ±      | 0  | 0±       | 0  | 0±       | 0  | 0土       | 0  | 0 <u>-+-</u> | 0  |      |
| 640 ppm    | <b>34</b> ±            | 1  | 33±.     | 1  | $32\pm$  | 1  | 30±      | 1  | 30±      | 1  | 29±          | i  |      |
| 600 ppm    | 83±                    | 2  | 81±      | 3  | 78±      | 1  | 74±      | 2  | 73±      | 2  | 70±          | 2  |      |
| 4000 ppm   | 209±                   | 6  | 205±     | 3  | 196±     | 4  | 189±     | 6  | $182\pm$ | 3  | 182±         | 7  |      |
| 7000 ppm   | $349\pm$               | 9  | 347±     | 11 | $336\pm$ | 13 | $324\pm$ | 13 | 318±     | 12 | 314土         | 10 |      |
| 10000 ppm  | 506土                   | 15 | $507\pm$ | 14 | 486±     | 19 | $461\pm$ | 15 | 459±     | 13 | $450\pm$     | 12 |      |

(HAN300)

BAIS 4

TABLE E 2

### CHEMICAL INTAKE CHANGES: FEMALE

STUDY NO. : 0745 ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj] UNIT : mg/kg/day REPORT TYPE : A1 13 SEX : FEMALE

#### CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANIMALS

PAGE : 3

| Group Name | Adminis      | tration | (weeks)  |    |         |    |              |                |          |    |              |    |         |    |  |
|------------|--------------|---------|----------|----|---------|----|--------------|----------------|----------|----|--------------|----|---------|----|--|
|            | 1            |         | 2        |    | 3       |    | 4            |                | 5        |    | 6            |    | 7       |    |  |
| Control    | 0 <u>:1-</u> | 0       | 0土       | 0  | 0±      | 0  | 0 <u>-ŀ-</u> | 0 <sup>.</sup> | 0±       | 0  | 0 ±-         | 0  | 0±      | 0  |  |
| 640 ppm    | 59±          | 2       | $54\pm$  | 2  | $51\pm$ | 2  | 48±          | 2              | 46±      | 2  | 43±          | 1  | $42\pm$ | 2  |  |
| 1600 ppm   | 144±         | 4       | 136±     | 8  | 123±    | 6  | $116\pm$     | 6              | 112±     | 5  | 103±         | 5  | 101±    | 5  |  |
| 4000 ppm   | 348±         | 6       | $335\pm$ | 15 | 314±    | 12 | 299±         | 9              | 292±     | 12 | 271±         | 12 | 272±    | 12 |  |
| 7000 ppm   | $549\pm$     | 21      | 562土     | 19 | 515土    | 15 | $483\pm$     | 17             | 471土     | 33 | <b>44</b> 8± | 31 | 421±    | 9  |  |
| 10000 ppm  | 733±         | 36      | $828\pm$ | 34 | 738±    | 25 | $681\pm$     | 35             | $649\pm$ | 30 | $613\pm$     | 29 | 600±    | 31 |  |
|            |              |         |          |    |         |    |              |                |          |    |              |    |         |    |  |

(HAN300)

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BAIS 4

STUDY NO. : 0745 ANIMAL : RAT F344/DuCr1Cr1;[F344/DuCrj] UNIT : mg/kg/day REPORT TYPE : A1 13 SEX : FEMALE

#### CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANIMALS

PAGE : 4

| roup Name | Adminis  | stration | (weeks)     |    |          |    |          |      |          |    |          |    |  |
|-----------|----------|----------|-------------|----|----------|----|----------|------|----------|----|----------|----|--|
|           | 8        |          | 9           |    | 10       |    | 11       |      | 12       |    | 13       |    |  |
| ontrol    | 0±       | 0        | 0±          | 0  | 0土       | 0  | 0±       | 0    | 0±       | 0  | 0±       | 0  |  |
| .40 ppm   | 39±      | 2        | <b>39</b> ± | 1  | 38±      | 1  | 36±      | 1    | 36±      | 2  | 35±      | 1  |  |
| 600 ppm   | 94±      | 4        | 93±         | 5  | 92±      | 7  | 88±      | 7    | 89±      | 6  | 85±      | 6  |  |
| 000 ppm   | 253±     | 9        | 250±        | 9  | 242±     | 10 | $237\pm$ | 5    | $232\pm$ | 9  | $232\pm$ | 5  |  |
| 000 ppm   | 413±     | 23       | 403±        | 17 | $393\pm$ | 17 | 380±     | • 16 | 379±     | 16 | 374土     | 20 |  |
| 0000 mgg  | $565\pm$ | 26       | $558\pm$    | 23 | $547\pm$ | 18 | $532\pm$ | 20   | 522±     | 14 | $521\pm$ | 18 |  |

(HAN300)

### TABLE F 1

### HEMATOLOGY: MALE

| STUDY NO. : 0745   |                        |
|--------------------|------------------------|
| ANIMAL : RAT F344/ | /DuCrlCrlj[F344/DuCrj] |
| MEASURE. TIME : 1  |                        |
| SEX : MALE         | REPORT TYPE : AI       |

### HEMATOLOGY (SUMMARY) ALL ANIMALS ( 14W)

| MEASURE. TIME :<br>SEX : MALE |                   | TYPE : AI                      |                |                  |        |               |        |            |      |            |        |              |        |                   | PAGE : |
|-------------------------------|-------------------|--------------------------------|----------------|------------------|--------|---------------|--------|------------|------|------------|--------|--------------|--------|-------------------|--------|
| Group Name                    | NO. of<br>Animals | RED BLO<br>1 O <sup>s</sup> /µ | DOD CELL<br>Le | HEMOGLO<br>g /dl |        | HEMATO<br>%   | CRIT   | MCV<br>f L |      | MCII<br>pg |        | MCHC<br>g∕dl |        | PLATELE<br>1 0ª⁄µ |        |
| Control                       | 10                | 9.57±                          | 0.09           | 15.7土            | 0.1    | <b>44.</b> 8± | 0.5    | 46.8±      | 0.3  | 16.4±      | 0.1    | 35.0±        | 0.4    | 711±              | 61     |
| 640 ppm                       | 10                | 9.48±                          | 0. 17          | 15.6±            | 0.3    | 44.6±         | 0.6    | 47.0±      | 0.4  | 16.5±      | 0.1    | 35. 1±       | 0.3    | 746±              | 69     |
| 1600 ppm                      | 10                | 9.51±                          | 0. 18          | 15.5±            | 0.2    | 44.4±         | 0.8    | 46.8±      | 0.3  | 16.3±      | 0.2    | 34.8±        | 0.4    | $785\pm$          | 42*    |
| 4000 ppm                      | 10                | 9.43±                          | 0.34*          | 15.2±            | 0.6**  | 43.8±         | 1.6**  | 46.4±      | 0.4  | 16.2±      | 0. 2** | 34.8±        | 0.4    | 803±              | 76**   |
| 7000 ppm                      | 10                | 9.15±                          | 0.21**         | 14.7土            | 0. 3** | 42.7±         | 1.1**  | 46.7土      | 0. 4 | 16. 1 ±    | 0.2**  | 34. 5±       | 0. 1** | 820±              | 43**   |
| 10000 ppm                     | 10                | 9.09±                          | 0.30**         | 14.8±            | 0. 4** | 42.9±         | 1. 3** | 47.2±      | 0. 4 | 16.3±      | 0.2    | 34.5±        | 0. 1** | 843±              | 43**   |

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STUDY NO. : 0745 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] MEASURE. TIME : 1 SEX : MALE REPORT TYPE : A1

NO. of

Animals

RETICULOCYTE

%

HEMATOLOGY (SUMMARY) ALL ANIMALS ( 14W)

METHEMOGLOBIN

%

#### • Control 10 1.7土 0.1 0.6 生 0.1 0.5± 0.2 640 ppm 10 1.7± 0.1 1.8± 0.2 0.6± 0.1 1600 ppm 10 10 0.7± 0.2 4000 ppm $2.3\pm$ 0.2\*\* 7000 ppm 10 2.5 ± 0.3\*\* 0.7± 0.1 10000 ppm 10 $2.6\pm$ 0.3\*\* 0.9± 0.2\*\* Significant difference ; \* : P ≦ 0.05 \*\* : P ≦ 0.01 Test of Dunnett

(HCL070)

Group Name

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PAGE : 2

STUDY NO. : 0745 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] MEASURE. TIME : 1 SEX : MALE REPORT TYPE : A1

### HEMATOLOGY (SUMMARY) ALL ANIMALS ( 14W)

| Group Name | NO. of<br>Animals | WBC<br>1 0 <sup>3</sup> /µl | Dif<br>NEUTRO | ferential | WBC (%<br>LYMPHO | ,) | MONO   |          | EOSINO |   | BASO |   | OTHER |   |    |
|------------|-------------------|-----------------------------|---------------|-----------|------------------|----|--------|----------|--------|---|------|---|-------|---|----|
| ontrol     | 10                | 7.22± 1.28                  | 22 ±-         | 4         | 74±              | 5  | 2±     | 1        | 1土     | 0 | 0±   | 0 | 1土    | 0 |    |
| 011101     | 10                | 1.88 - 1.80                 | <u> </u>      |           | 11-              | •  | 8-     | 1        |        | Ŭ | •=   | Ū |       | Ū |    |
| 640 ppm    | 10                | 7.74± 1.61                  | 21±           | 4         | 75±              | 4  | $2\pm$ | l        | 1±     | 0 | 0±.  | 0 | 1±    | 0 |    |
| .600 ppm   | 10                | $7.60 \pm 1.85$             | $23\pm$       | 5         | 73±              | 5  | $2\pm$ | 0        | 1±     | 0 | 0±   | 0 | 1±    | 0 |    |
| 000 ppm    | 10                | 7.40± 1.17                  | 21±           | 2         | 75±              | 2  | 2±     | 0        | 1±     | 0 | 0±   | 0 | 1±    | 0 |    |
| mqq 000    | 10                | 7.84± 1.84                  | 21土           | 2         | 75±              | 2  | 2±     | 0        | 上      | 0 | 0 ±- | 0 | 1±    | 0 |    |
| 0000 ppm   | 10                | $7.56 \pm 1.54$             | 20±           | 2         | 76±              | 3  | $2\pm$ | 0.       | 1±     | 0 | 0±   | 0 | 1±    | 0 |    |
| Significan | t difference ;    | * : P ≦ 0.05                | ** : P ≦      | 0.01      |                  |    | Test   | of Dunne | ett    |   |      |   |       |   |    |
| HCL070)    |                   |                             |               |           |                  |    |        |          |        |   |      |   |       |   | BA |

PAGE : 3

### TABLE F 2

## HEMATOLOGY: FEMALE

| EX : FEMALE | REPORT            | TYPE : A1                   |                |                 |        |                   |       |                   |       |           |       |               |       |                                | PAGE : |
|-------------|-------------------|-----------------------------|----------------|-----------------|--------|-------------------|-------|-------------------|-------|-----------|-------|---------------|-------|--------------------------------|--------|
| Group Name  | NO. of<br>Animals | RED BL<br>10 <sup>6</sup> / | 00D CELL<br>µl | HEMOGLO<br>g∕dl |        | HEMATOO<br>%      | CRIT  | MCV<br>f <b>l</b> |       | MCH<br>Þg |       | MCIIC<br>g∕dl |       | PLATELE<br>1 O <sup>a</sup> ⁄µ |        |
| ontrol      | 10                | 8. 70 <u>-1</u> -           | 0.20           | 15.5±           | 0.3    | 42. 7 <u>-1</u> - | 0. 9  | 49.1±             | 0.3   | 17.8土     | 0.2   | 36.3±         | 0. 3  | 794土                           | 54     |
| 40 ppm      | 10                | 8.65±                       | 0. 22          | 15.4±           | 0.4    | 42.4±             | 1.0   | 49.0±             | 0.2   | 17.7±     | 0.2   | 36.2±         | 0.3   | 826±                           | 37     |
| 500 ppm     | 10                | 8.52±                       | 0. 15          | 15.1±           | 0.3*   | 41.8±             | 0.9   | 49.1±             | 0.5   | 17.7±     | 0.1   | 36.2±         | 0.4   | 879±                           | 26**   |
| 000 ppm     | 10                | 8.23±                       | 0. 19**        | 14.5±           | 0. 3** | 40.9±             | 0.9** | 49.7±             | 0.3** | 17.6±     | 0.1*  | 35.4±         | 0.4** | 879±                           | 47**   |
| )00 ppm     | . 10              | 8. 03 <u>-1-</u>            | 0.20**         | 13.9土           | 0.3**  | 40. l±            | 0.9** | 49. 9-1-          | 0.4** | 17.3±     | 0.2** | 34.7±         | 0.3** | $937\pm$                       | 44**   |
| mqq 0000    | 10                | 8.17±                       | 0. 22**        | 14.1±           | 0.3**  | 40.9±             | 1.1** | 50.1±             | 0.5** | 17.3±     | 0.2** | 34.5±         | 0.3** | 945±                           | 63**   |

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STUDY NO. : 0745 ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj] MEASURE. TIME : 1 SEX : FEMALE REPORT TYPE : AI

### HEMATOLOGY (SUMMARY)

#### ALL ANIMALS ( 14W)

PAGE : 5

1-1-1-

| Group Name | NO. of<br>Animals | RETICUL<br>%    | .OCYTE | METHEMO<br>% | LOBIN | N. |
|------------|-------------------|-----------------|--------|--------------|-------|----|
| Control    | 10                | 1.5±            | 0. 1   | 0.7±         | 0. 2  |    |
| 640 ppm    | 10                | 1.7±            | 0. 2   | 0.7±         | 0. 2  |    |
| 1600 ppm   | 10                | 2.1±            | 0. 4** | 0.7±         | 0. 2  |    |
| 4000 ppm   | 10                | 2.4±            | 0. 2** | 0.9±         | 0. 2  |    |
| 7000 ppm   | 10                | 3.7 <u>-1</u> - | 0. 6** | 1.0土         | 0. 1* |    |
| 10000 թթտ  | 10                | 4.0±            | 0.5**  | 1.0±         | 0.3*  |    |

(HCL070)

|                               | AT F344/DuCrlCr   | :1 j [F344/Du             | ıCrj]  |               |          | HEMATOLOG<br>ALL ANIMA |     |      |          |        |   |        |   |       |   |          |
|-------------------------------|-------------------|---------------------------|--------|---------------|----------|------------------------|-----|------|----------|--------|---|--------|---|-------|---|----------|
| MEASURE. TIME<br>SEX : FEMALE |                   | TYPE : AI                 | L      |               |          |                        |     |      |          |        |   |        |   |       |   | PAGE : 6 |
| Group Name                    | NO. of<br>Animals | ₩B(<br>1 0 <sup>3</sup> / |        | Dif<br>NEUTRO | ferentia | 1 WBC (%<br>Lympho     | 5)  | MONO |          | EOSINO |   | BASO   |   | OTHER |   | •        |
| Control                       | 10                | 4.54±                     | 0.56   | 21土           | 2        | 74±                    | 2   | 3±   | 1        | 1±     | 0 | 0土     | 0 | 1土    | 0 |          |
| 640 ppm                       | 10                | 4.38±                     | 1. 02  | 20±           | 4        | 76±                    | 4   | 2±.  | 0        | 1±     | 0 | 0±     | 0 | 1±    | 0 |          |
| 1600 ppm                      | 10                | 4.51±                     | 1.05   | 23±           | 8        | 73±                    | 8   | 2±   | 0        | 1±     | 0 | 0±     | 0 | . 1±  | 0 |          |
| 4000 ppm                      | 10                | 4.63±                     | 0.99   | 19土           | 3        | 77±                    | . 3 | 2±   | 0**      | 1±     | 0 | 0±     | 0 | 1±    | 1 |          |
| 7000 ppm                      | 10                | 5.29±                     | 0.85   | 19土           | 3        | 78±                    | 3   | 2土   | 0*       | 1±     | 0 | 0±     | 0 | 1±    | 0 |          |
| 10000 µµm                     | 10                | 5.58±                     | 1. 09  | 18±           | 3        | <b>7</b> 8±            | 3   | 2±   | 0**      | 1±     | 0 | $0\pm$ | 0 | 2±    | 1 |          |
| Significan                    | it difference ;   | *:P:                      | ≤ 0.05 | ** : P ≦      | 0.01     |                        |     | Test | of Dunne | ett    |   |        |   |       |   |          |
| (HCL070)                      |                   |                           |        |               |          |                        |     |      |          |        |   |        |   |       |   | BAIS 4   |

### TABLE G 1

## BIOCHEMISTRY: MALE

 STUDY NO. : 0745
 BIOCHEMISTRY (SUMMARY)

 ANIMAL
 : RAT F344/DuCr1Cr1j[F344/DuCrj]

 MEASURE. TIME : 1
 SEX : MALE

 REPORT TYPE : A1

T-BILIRUBIN GLUCOSE T-CHOLESTEROL TRIGLYCERIDE NO. of TOTAL PROTEIN ALBUMIN A/G RATIO Group Name mg∕dℓ mg∕dℓ mg∕dl mg∕dℓ Animals g / dl g∕dl 3.4± 0.1 1.1土 0.0 0.10± 0.01 178± 10  $61\pm$ 4 60 <u>-1-</u> 1310 6.6± 0.2 Control  $176\pm$  $72\pm$  $66 \pm$ 24 640 ppm 10 6.7± 0.1 3.6± 0.0\*\* 1.1± 0.1 0.11± 0.01 11 5\*\* 10 3.7± 0.1\*\* 1.1± 0.1 0.10± 0.01  $186 \pm$ 12  $83\pm$ 6\*\* 75± 25 1600 ppm 6.9± 0.2\*\* 4000 ppm 10  $7.2 \pm$ 0.2\*\* 3.9± 0.1\*\* 1.2± 0.1 0.12± 0.01\*\*  $182\pm$ 6  $108 \pm$ 7\*\*  $66\pm$ 25 0.14± 0.01\*\*  $179\pm$ 10 112土 8\*\* 52± 19 7000 ppm 10 7.3± 0.1\*\*  $3.9\pm$ 0.1\*\*  $1.2 \pm$ 0.1 13 10000 ppm 10 7.4± 0.2\*\* 4.0± 0.1\*\* 1.2± 0.0\*\* 0.14± 0.01\*\*  $172\pm$ 10  $113\pm$ 8\*\*  $38\pm$ 

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

Test of Dunnett

(HCL074)

BAIS 4

#### PAGE : 1

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| STUDY NO. : 074<br>ANIMAL : RAT<br>MEASURE. TIME :<br>SEX : MALE | T F344/DuCrlCrlj<br>: 1 |                  | i]    |              | B1<br>AL | OCHEMISTRY (<br>L ANIMALS ( | SUMMARY)<br>14W) |              |      |                    |      |               |   |             | PAGE : 2 |  |
|------------------------------------------------------------------|-------------------------|------------------|-------|--------------|----------|-----------------------------|------------------|--------------|------|--------------------|------|---------------|---|-------------|----------|--|
| Group Name                                                       | NO. of<br>Animals       | PHOSPHC<br>mg/dl |       | AST<br>IU/   | L        | ALT<br>IU/A                 | · · · · · ·      | LDH<br>IU⁄£  |      | ALP<br>IU/S        | 2    | G-GTP<br>IU∕£ |   | CK<br>IU/J  | ٤        |  |
| Contro1                                                          | 10                      | 114±             | 7     | 144土         | 33       | 72土                         | 13               | $166\pm$     | 41   | 396±               | 36   | I <u>+</u>    | 0 | 105土        | 19       |  |
| 640 ppm                                                          | 10                      | 128±             | 8*    | 119±         | 45       | 60±                         | 18               | $137\pm$     | 38   | 361±               | 27*  | 1±            | 1 | 97±         | 12       |  |
| 1600 ppm                                                         | 10                      | $145\pm$         | 9**   | 112±         | 32       | 59±                         | 12               | 137±         | 46   | 345土               | 17** | 1土            | 1 | 103±        | 13       |  |
| 4000 ppm                                                         | 10                      | 177±             | 16**  | 103±         | 34*      | $55\pm$                     | 16*              | 131±         | 44   | 308±               | 25** | 1±            | 1 | 93±         | 19       |  |
| 7000 ppm                                                         | 10                      | 180土             | 14**  | 90土          | 30**     | 43±                         | 11**             | 121 ±        | 50   | 293 <del>+</del> - | 26** | 1±            | 1 | 93 <u>±</u> | 28       |  |
| 10000 ppm                                                        | 10                      | 183±             | 14**  | 71±          | 16**     | 34±                         | 6**              | 94±          | 28** | $282\pm$           | 31** | 2±            | 1 | 88±         | 16       |  |
| Significan                                                       | t difference ;          | * : P ≦ 0        | ). 05 | ** : P ≦ 0.( | )1       |                             |                  | Test of Dunn | ett  |                    |      |               |   |             |          |  |
| (IICL074)                                                        |                         |                  |       |              |          |                             |                  |              |      |                    |      |               |   |             | BAIS 4   |  |

STUDY NO. : 0745 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] MEASURE. TIME : 1 SEX : MALE REPORT TYPE : AI

NO. of

UREA NITROGEN

CREATININE

#### BIOCHEMISTRY (SUMMARY) ALL ANIMALS ( 14W)

SODIUM

#### mg∕dℓ mg∕dℓ mEq∕ℓ mEq∕£ mEq∕ℓ mg∕dl mg∕dl Animals 3.6± 0.3 10. 4 ± 0.2 5.4土 0.8 · 10 18.9 生 1.1 $0.5\pm$ 0.0 $142\pm$ 1 106土 1 10 18.8± 1.1 0.5± 0.0 $142\pm$ $3.7\pm$ 0.2 $105\pm$ 1 10.4± 0.2 5.4± 0.7 1 10.7± $5.5\pm$ 0.6 1600 ppm 10 19.3± 1.1 0.5± 0.0 $142\pm$ 0 $3.8\pm$ 0.3 $105\pm$ 1 0.1\*\* 5.4± 0.6 0.3 $105\pm$ 10.8± 0.1\*\* 4000 ppm 10 21.5± 1.6\*\* 0.6± 0.1 $141 \pm$ 1 3.8± 1 7000 ppm 10.9± 10 0.6土 0.0 $142\pm$ 3.8± 0.2 104± 0.1\*\* 5.4± 0.4 $21.9 \pm$ 1.5\*\* 1 1 5.3± 0.4 11.0± 0.3\*\* 10000 ppm 10 $21.8\pm$ 2.1\*\* 0.6± 0.1 $142\pm$ 1 $3.8\pm$ 0.2 104± 1\* Significant difference ; $*: P \leq 0.05$ \*\* : P ≦ 0.01 Test of Dunnett

POTASSIUM

CHLORIDE

CALCIUM

(HCL074)

Group Name

Control

640 ppm

BAIS 4

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INORGANIC PHOSPHORUS

### TABLE G 2

## **BIOCHEMISTRY: FEMALE**

STUDY NO. : 0745 ANIMAL : RAT F344/DuCr1Cr1;[F344/DuCr;] MEASURE. TIME : 1 SEX : FEMALE REPORT TYPE : A1

#### BIOCHEMISTRY (SUMMARY) ALL ANIMALS (14W)

| Group Name | NO. of<br>Animals | TOTAL F<br>g∕dl | PROTEIN | albumin<br>g ⁄dl | 1      | A/G RAT  | °10 | T-BILI<br>mg∕dl |         | GLUCOSE<br>mg∕dl |    | T−CHOLE<br>mg∕dℓ | STEROL | TRIGLYCI<br>mg∕dl | RIDE |
|------------|-------------------|-----------------|---------|------------------|--------|----------|-----|-----------------|---------|------------------|----|------------------|--------|-------------------|------|
| Control    | 10                | 6.3土            | 0.2     | 3.4⊥-            | 0. 1   | 1.2±     | 0.1 | 0.11±           | 0.01    | 141 ±            | 14 | 67±              | 6      | 14土               | 4    |
| 640 ppm    | 10                | 6.4±            | 0.2     | 3.5±             | 0. 1   | 1.2±     | 0.1 | 0.11±           | 0.01    | 148±             | 11 | 80±              | 6**    | 16±               | 5    |
| 1600 ppm   | 10                | 6.7±            | 0.2**   | 3.6±             | 0.1**  | 1.2±     | 0.1 | 0.13±           | 0.01**  | $152\pm$         | 6  | 95±              | 6**    | 17±               | 4    |
| 000 ppm    | 10                | 6.8±            | 0.2**   | 3.7±             | 0. 1** | 1.2±     | 0.0 | 0.17±           | 0.02**  | 145±             | 12 | 116±             | 10**   | 14土               | 3    |
| 000 ppm    | 10                | 6. 9±           | 0. 2**  | 3.8土             | 0. 1** | $1.2\pm$ | 0.1 | 0.20±           | 0. 03** | 150 ±            | 7  | 124±             | 12**   | 15土               | 1    |
| mqq 0000.  | 10                | 6.9±            | 0.2**   | 3.8±             | 0.1**  | 1.2±     | 0.1 | 0.17±           | 0.01**  | 147±             | 5  | 126±             | 10**   | 13±               | 2    |

(HCL074)

BAIS 4

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| roup Name | NO. of<br>Animals | PHOSPHO<br>mg∕dℓ | LIPID | AST<br>IU/S | !  | ALT<br>IU⁄\$ | 2  | LDH<br>IU⁄J | 2  | ALP<br>IU/S | 2    | G−GTP<br>IU∕£ |     |      |    |
|-----------|-------------------|------------------|-------|-------------|----|--------------|----|-------------|----|-------------|------|---------------|-----|------|----|
| ontrol    | 10                | 131±             | 12    | 74±         | 6  | 37土          | 7  | 91土         | 22 | 271±        | 28   | 1±            | 0   | 100土 | 15 |
| 40 ppm    | 10                | 149±             | 11*   | . 74±       | 13 | 39±          | 8  | 96±         | 16 | $259\pm$    | 22   | 1±            | 0   | 97±  | 12 |
| 500 ppm   | 10                | 166±             | 13**  | 83±         | 16 | 43±          | 8  | 113±        | 31 | $251\pm$    | 26   | 2±            | 0   | 100± | 13 |
| 000 ppm   | 10                | 187±             | 15**  | 84±         | 33 | 48±          | 21 | 116±        | 39 | 233±        | 28** | 2±            | 1   | 101± | 15 |
| 100 ppm   | 10                | 191土             | 18**  | 72 ±        | 15 | 33土          | 8  | 107 ±       | 21 | $233\pm$    | 15** | $2\pm$        | ]** | 90土  | 14 |
| 1000 ppm  | 10                | 194土             | 13**  | 64±         | 8  | $32\pm$      | 3  | 101±        | 19 | $260\pm$    | 32   | 2±            | 1** | 94±  | 19 |

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(IICL074)

BAIS 4

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STUDY NO. : 0745 ANTMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] MEASURE. TIME : 1 SEX : FEMALE REPORT TYPE : A1

### BIOCHEMISTRY (SUMMARY)

#### ALL ANIMALS ( 14W)

| Group Name | NO. of<br>Animals | UREA NI<br>mg∕dℓ | TROGEN | CREATIN<br>mg⁄dl |      | SODIUM<br>mEq∕£ |   | POTASSI<br>mEq⁄. |     | CHLORIDE<br>mEq∕£ |   | CALCIU<br>mg⁄dl |        | INORGAN<br>mg∕dl | KIC PHOSPHORU |
|------------|-------------------|------------------|--------|------------------|------|-----------------|---|------------------|-----|-------------------|---|-----------------|--------|------------------|---------------|
| Control    | 10                | 16.4±            | 2. 3   | 0.6±             | 0. 1 | 142±            | 1 | 3.5±             | 0.2 | 107土              | 1 | 10. 0±          | 0.3    | 4. 7-느           | 1. 1          |
| 540 ppm    | 10                | 17.9±            | 1.9    | 0.6±             | 0. 1 | 142±            | 1 | 3.3±             | 0.2 | 107±              | 1 | 10.1±           | 0.2    | 4.4土             | 1. 1          |
| .600 ppm   | 10                | 18.6±            | 1.7    | 0.5±             | 0.0  | 143±            | 1 | 3.4±             | 0.3 | 106±              | 2 | 10.3±           | 0.1**  | 4.8±             | 1. 1          |
| .000 ppm   | 10                | 18.3±            | 1.2    | 0.6±             | 0.0  | 142±            | I | 3.4±             | 0.3 | 107±              | 1 | 10.3±           | 0.2**  | 4.5±             | 1.0           |
| 000 ppm    | 10                | 21.0±            | 1.9**  | 0.6±             | 0.0  | 142土            | 1 | 3.4±             | 0.3 | 107±              | 2 | 10. 4 ±         | 0. 1** | 4.8±             | 0.6           |
| .0000 mgg  | 10                | 22.3±            | 3. 3** | 0.5±             | 0.0  | 142±            | 1 | 3.8±             | 0.3 | $106\pm$          | 2 | 10.6±           | 0. 2** | 5.0±             | 0.4           |

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

(IICL074)

Test of Dunnett

### TABLE H 1

### URINALYSIS: MALE

#### Urinalysis of male rats

In the dosed groups, pH, protein, ketone body and bilirubin could not be measured by urine test paper in some animals, because their urine were colored by metabolite of test substance.

The inspection items and number of animals that could not be measured are shown as followed.

pH: 4000 ppm(1), 7000 ppm(6), 10000 ppm(9)

Protein: 1600 ppm(5), 4000 ppm(9), 7000 ppm and 10000 ppm(10)

Ketone body: 1600 ppm(1), 4000 ppm(5), 7000 ppm(7), 10000 ppm(10)

Bilirubin: 1600 ppm(6), 4000 ppm(9), 7000 ppm and 10000 ppm(10)

Therefore, pH and ketone body in 10000 ppm dosed group, protein and bilirubin in 4000 ppm and above dosed groups could not be evaluated.

STUDY NO. : 0745 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] MEASURE. TIME : 1 SEX : MALE REPORT TYPE : A1

#### URINALYSIS

| Group Name | NO. of       | pH       |     |       |     |      |     |      |     | Protein        |      | Glucose               | Ketone body        | Bilirubin      |
|------------|--------------|----------|-----|-------|-----|------|-----|------|-----|----------------|------|-----------------------|--------------------|----------------|
| _          | 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 | - ± + 2+ 3+ 4+ CHI | - + 2+ 3+ CIII |
|            | 10           | <u>^</u> |     |       |     |      |     | 0    |     |                |      | 10 0 0 0 0 0          |                    | 10 0 0 0       |
| Control    | 10           | 0        | 0   | 0     | 0   | 0    | 2   | 8    |     | 0 0 6 4 0 0    |      | 10 0 0 0 0 0          | 1 9 0 0 0 0        | 10 0 0 0       |
| 640 ppm    | 10           | 0        | 0   | 0     | 0   | 0    | 8   | 2    | **  | 0 0 9 1 0 0    |      | 10 0 0 0 0 0          | 2 8 0 0 0 0        | 10 0 0 0       |
| 1600 ppm   | 10           | 0        | 0   | 0     | 0   | 1    | 9   | 0    | **  | 0 1 4 0 0 0    |      | 10 0 0 0 0 0          | 1 8 0 0 0 0        | 4 0 0 0        |
| 4000 ppm   | 10           | 0        | 0   | 0     | 0   | 1    | 8   | 0    | **  | 0 1 0 0 0 0    | ?    | 10 0 0 0 0 0          | 1 4 0 0 0 0        | 1000?          |
| 7000 ppm   | 10           | 0        | 0   | 0     | 0   | 0    | 4   | 0    | **  | 0 0 0 0 0 0    |      | 10 0 0 0 0 0          | 0 3 0 0 0 0        | 0 0 0 0        |
| 10000 ppm  | 10           | 0        | 0   | 0     | 0   | 0    | 1   | 0    | ?   | 0 0 0 0 0 0    |      | 10 0 0 0 0 0          | 0 0 0 0 0 0        | 0 0 0 0        |
|            |              |          |     |       |     |      |     |      |     |                |      |                       |                    |                |
| Significan | t difference | *:       | P≦  | 0. 05 | 5   | ** : | ץ ≦ | 0.01 |     |                | Test | of CHI SQUARE         |                    |                |

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

(HCL101)

| EASURE. TIME : 1<br>EX : MALE REPORT TYPE : AL |                   |                                   |                                  |  | PAGE : 2 |
|------------------------------------------------|-------------------|-----------------------------------|----------------------------------|--|----------|
| Group Name                                     | NO. of<br>Animals | Occult blood<br>$-\pm +2+3+$ CIII | Urobilinogen<br>± 1 2+ 3+ 4+ CHI |  | •        |
|                                                |                   |                                   |                                  |  |          |
| Control                                        | 10                | 10 0 0 0 0                        | 10 0 0 0 0                       |  |          |
| 640 ppm                                        | 10                | 10 0 0 0 0                        | 10 0 0 0 0                       |  |          |
| 1600 ppm                                       | 10                | 10 0 0 0 0                        | 10 0 0 0 0                       |  |          |
| 4000 ppm                                       | 10                | 10 0 0 0 0                        | 10 0 0 0 0                       |  |          |
| 7000 ppm                                       | 10                | 10 0 0 0 0                        | 10 0 0 0 0                       |  |          |
| 10000 ppm                                      | 10                | 10 0 0 0 0                        | 10 0 0 0 0                       |  |          |
|                                                |                   |                                   |                                  |  |          |

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(HCL101)

### TABLE H 2

### URINALYSIS: FEMALE

### Urinalysis of female rats

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In the dosed groups, pH, protein, ketone body and bilirubin could not be measured by urine test paper in some animals, because their urine were colored by metabolite of test substance.

The inspection items and number of animals that could not be measured are shown as followed.

pH: 7000 ppm(1), 10000 ppm(2)

Protein: 4000 ppm(8), 7000 ppm and 10000 ppm(10)

Ketone body: 1600 ppm(1), 4000 ppm(7), 7000 ppm and 10000 ppm(10)

Bilirubin: 1600 ppm(1), 4000 ppm(6), 7000 ppm and 10000 ppm(10)

Therefore, protein in 4000 ppm and above dosed groups, ketone body and bilirubin in 7000 ppm and above dosed groups could not be evaluated.

| STUDY NO. | : 0745                           |  |
|-----------|----------------------------------|--|
| ANIMAL    | : RAT F344/DuCr1Cr1j[F344/DuCrj] |  |
| MEASURE.  | TIME : 1                         |  |
| SEX : FEN | IALE REPORT TYPE : A1            |  |

URINALYSIS

PAGE : 3

| Group Name | NO. of  | -   |     |     |     |     |     |         | Prot | ein |     |      |      |     | Glu | 1005 | e   |      |          | Ket | ton | Ketone body |    |    |        | Bilirubin |   |      |       |
|------------|---------|-----|-----|-----|-----|-----|-----|---------|------|-----|-----|------|------|-----|-----|------|-----|------|----------|-----|-----|-------------|----|----|--------|-----------|---|------|-------|
|            | Animals | 5.0 | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 CHI | - ,; | ± - | + 2 | + 3- | + 4+ | CHI |     | ±    | + : | 2+ 3 | + 4+ CHI | _   | ±   | +           | 2+ | 3+ | 4+ CHI | -         | + | 2+ 3 | + CHI |
| Control    | 10      | 0   | 0   | 0   | 0   | 0   | 1   | 6       | 0    | 2   | 8   | 0 (  | ) 0  |     | 10  | 0    | 0   | 0    | 0 0      | 7   | 3   | 0           | 0  | 0  | 0      | 10        | 0 | 0    | 0     |
| 540 ppm    | 10      | 0   | 0   | 0   | 0   | 1   | 5   | 4       | 0    | 7   | 3   | 0 (  | ) 0  | *   | 10  | 0    | 0   | 0    | 0 0      | 8   | 2   | 0           | 0  | 0  | 0      | 10        | 0 | 0    | 0     |
| 1600 ppm   | 10      | 0   | 0   | 0   | 0   | 1   | 6   | 3       | 0    | 7   | 3   | 0 (  | ) 0  | *   | 10  | 0    | 0   | 0    | 0 0      | 6   | 3   | 0           | 0  | 0  | 0      | 9         | 0 | • 0  | 0     |
| 4000 ppm   | 10      | 0   | 0   | 0   | 0   | 0   | 5   | 5       | 0    | 1   | 1   | 0 (  | 0    | ?   | 10  | 0    | 0   | 0    | 0 0      | 3   | 0   | 0           | 0  | 0  | 0      | 4         | 0 | 0    | 0     |
| 7000 ppm   | 10      | 0   | 0   | 0   | 0   | 2   | 3   | 4       | 0    | 0   | 0   | 0 (  | ) 0  |     | 10  | 0    | 0   | 0    | 0 0      | 0   | 0   | 0           | 0  | 0  | 0      | 0         | 0 | 0    | 0     |
| 10000 µµm  | 10      | 0   | 0   | 0   | 0   | 0   | 5   | 3       | 0    | 0   | 0   | 0 0  | ) 0  |     | 10  | 0    | 0   | 0    | 0 0      | 0   | 0   | 0           | 0  | 0  | 0      | 0         | 0 | 0    | D     |

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

(HCL101)

| SEX : FEMALE | REPORT            | TYPE : A1                          |                                        | PAGE : 4 |  |
|--------------|-------------------|------------------------------------|----------------------------------------|----------|--|
| Group Name   | NO. of<br>Animals | Occult blood<br>$- \pm + 2+ 3+$ CH | Urobilinogen<br>I $\pm$ + 2+ 3+ 4+ CHI |          |  |
|              |                   |                                    |                                        |          |  |
| Control      | 10                | 10 0 0 0 0                         | 10 0 0 0 0                             |          |  |
| 640 ppm      | 10                | 10 0 0 0 0                         | 10 0 0 0 0                             |          |  |
| 1600 ppm     | 10                | 10 0 0 0 0                         | 10 0 0 0 0                             |          |  |
| 4000 ppm     | 10                | 10 0 0 0 0                         | 10 0 0 0 0                             |          |  |
| 7000 ppm     | 10                | 10 0 0 0 0                         | 10 0 0 0 0                             | . ·      |  |
| 10000 ppm    | 10                | 10 0 0 0 0                         | 10 0 0 0 0                             | ·        |  |

BAIS 4

#### (HCL101)

TABLE I 1

## GROSS FINDINGS: MALE: ALL ANIMALS

| STUDY NO.<br>ANIMAL<br>REPORT TYP<br>SEX | : 0745<br>: RAT F344/DuCr1Cr1j[F344/DuCrj]<br>PE : A1<br>: MALE | GROSS FINDINGS (SUMMARY)<br>ALL ANIMALS (O- 14W) |                   |                   |                    | PAGE : 1           |
|------------------------------------------|-----------------------------------------------------------------|--------------------------------------------------|-------------------|-------------------|--------------------|--------------------|
| Organ                                    | _ Findings                                                      | Group Name<br>NO. of Animals                     | Control<br>10 (%) | 640 ppm<br>10 (%) | 1600 ppm<br>10 (%) | 4000 ppm<br>10 (%) |
| liver                                    | herniation                                                      |                                                  | 0 ( 0)            | 2 (20)            | 2 (20)             | 1 (10)             |

(HPT080)

BAIS 4

| STUDY NO.<br>ANIMAL<br>REPORT TYPE<br>SEX | : 0745<br>: RAT F344/DuCr1Cr1j[F344/DuCrj] | GROSS FINDINGS (SUMMARY)<br>ALL ANIMALS (0- 14W) |                    |                     | PAGE : 2 |
|-------------------------------------------|--------------------------------------------|--------------------------------------------------|--------------------|---------------------|----------|
| Organ                                     | Findings                                   | Group Name<br>NO. of Animals                     | 7000 ррш<br>10 (%) | 10000 ррм<br>10 (%) |          |
| liver                                     | herniation                                 |                                                  | 1 (10)             | 0 ( 0)              |          |

(HPT080)

TABLE I 2

## GROSS FINDINGS: FEMALE: ALL ANIMALS

# STUDY NO. : 0745 GROSS FINDINGS (SUMMARY) ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] ALL ANIMALS (0- 14W) REPORT TYPE : A1 SEX : FEMALE

| PAGE | : | 3 |
|------|---|---|
|      |   |   |

| Organ | Findings   | Group Name<br>NO. of Animals | Control<br>10 (%) | 640 ppm<br>10 (%) | 1600 ppm<br>10 (%) | 4000 ppm<br>10 (%) |
|-------|------------|------------------------------|-------------------|-------------------|--------------------|--------------------|
| liver | herniation |                              | 1 (10)            | 0 ( 0)            | 1 (10)             | 2 (20)             |
| ovary | cyst       |                              | 0 ( 0)            | 1 (10)            | 0 ( 0)             | 0 ( 0)             |
|       |            |                              |                   |                   |                    |                    |

(HPT080)

| STUDY NO.<br>ANIMAL<br>REPORT TYPI<br>SEX | : 0745<br>: RAT F344/DuCr1Cr1;[F344/DuCrj]<br>Ε : Λ1<br>: FEMALE | GROSS FINDINGS (SUMMARY)<br>ALL ANIMALS (O- 14W) | PAGE              | E: 4 |
|-------------------------------------------|------------------------------------------------------------------|--------------------------------------------------|-------------------|------|
| Organ                                     | Findings                                                         | Group Name 7000 ppm 1<br>NO. of Animals 10 (%)   | 000 ppm<br>10 (%) |      |
| liver                                     | herniation                                                       | 0 ( 0)                                           | 1 (10)            |      |
| ovary                                     | cyst                                                             | 0 ( 0)                                           | 0 ( 0)            |      |

(IIPT080)

### TABLE J 1

## ORGAN WEIGHT, ABSOLUTE: MALE

STUDY NO. : 0745 ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj] REPORT TYPE : A1 SEX : MALE UNIT: g

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

#### THYMUS ADRENALS TESTES HEART LUNGS Group Name NO. of Body Weight Animals $0.244 \pm 0.021$ 0.976± 0.049 Control 10 309土 7 0.049± 0.003 3.134± 0.131 0.963 ± 0.046 304± 11 $0.247 \pm 0.026$ $0.051 \pm 0.004$ 3.157± 0.071 0.944± 0.044 0.974± 0.054 10 640 ppm 307± 15 1600 ppm 10 0.229± 0.020 $0.052 \pm 0.005$ $3.253 \pm 0.104$ 0.969± 0.042 0.966± 0.051 10 299± 21 0.221± 0.021 0.051± 0.004 $3.335 \pm 0.292$ 0.906± 0.054\* 0.945± 0.039 4000 ppm 7000 ppm 10 276± 9\*\* 0.200± 0.016\*\* 0.050 ± 0.002 $3.317\pm$ 0.162\* 0.876土 0.031\*\* 0.919± 0.042\* 0.873± 0.050\*\* 10000 ppm 10 $258\pm$ 9\*\* 0.184± 0.016\*\* $0.048 \pm 0.003$ 3.294± 0.096\* 0.826± 0.046≠\*

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

Test of Dunnett

(HCL040)

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PAGE : 1

STUDY NO. : 0745 ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj] REPORT TYPE : A1 SEX : MALE UNIT: g

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

PAGE : 2

| Group Name | NO. of<br>Animals | KIDNEYS      | SPLEEN            | LIVER                   | BRAIN        |     |  |  |
|------------|-------------------|--------------|-------------------|-------------------------|--------------|-----|--|--|
|            |                   | · · ·        |                   |                         |              | • . |  |  |
| ontrol     | 10                | 1.906± 0.070 | $0.607 \pm 0.032$ | 7.478 $\pm$ 0.264       | 1.916± 0.037 |     |  |  |
| 40 ppm     | 10                | 1.891± 0.091 | 0.605± 0.030      | $7.932 \pm 0.530$       | 1.937± 0.059 |     |  |  |
| 1600 ppm   | 10                | 1.965± 0.081 | 0.607± 0.037      | 8.811± 0.455**          | 1.949± 0.057 |     |  |  |
| 4000 ppm   | 10                | 1.982± 0.160 | 0.626± 0.059      | 9.703± 0.883**          | 1.908± 0.039 |     |  |  |
| 000 ppm    | 10                | 1.946± 0.092 | 0.615± 0.032      | 9.451± 0.360 <b>*</b> * | 1.903土 0.053 |     |  |  |
| 0000 ppm   | 10                | 1.879± 0.100 | 0.604± 0.019      | 9.228± 0.483**          | 1.882± 0.039 |     |  |  |

(HCL040)

TABLE J 2

## ORGAN WEIGHT, ABSOLUTE: FEMALE

STUDY NO. : 0745 ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj] REPORT TYPE : A1 SEX UNI

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

| Group Name | NO. of<br>Animals | Body V | Veight | THYM   | US      | ADRE   | NALS  | OVAR    | IES      | HEAR   | Т       | LUNG   | S       |  |
|------------|-------------------|--------|--------|--------|---------|--------|-------|---------|----------|--------|---------|--------|---------|--|
| Control    | 10                | 176土   | 9      | 0.204± | 0. 030  | 0.056± | 0.004 | 0. 126± | 0.012    | 0.651± | 0. 027  | 0.722± | 0.024   |  |
| 640 ppm    | 10                | 173±   | . 9    | 0.194± | 0.027   | 0.057± | 0.006 | 0.137±  | 0. 058   | 0.646± | 0.061   | 0.719± | 0. 059  |  |
| 1600 ppm   | 10                | 167±   | 9*     | 0.183± | 0.020   | 0.056± | 0.004 | 0.116±  | 0.013    | 0.622± | 0.035   | 0.709± | 0.022   |  |
| 4000 ppm   | 10                | 157±   | 7**    | 0.185± | 0. 023  | 0.056± | 0.006 | 0.111±  | 0.020    | 0.609± | 0. 028* | 0.703± | 0. 047  |  |
| 7000 ppm   | 10                | 152±   | 5**    | 0.177± | 0.018   | 0.054± | 0.005 | 0.109±  | 0.013    | 0.583土 | 0.024** | 0.669± | 0.028** |  |
| 10000 ppm  | 10                | 150±   | 5**    | 0.161± | 0.016** | 0.052± | 0.005 | 0.100±  | 0. 016** | 0.556± | 0.025** | 0.658± | 0.041** |  |

(HCL040)

BAIS 4

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3

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

| Group Name | NO. of<br>Animals | KID    | NEYS     | SPL    | EEN     | LIV    | ER       | BRA        | IN      |  |  |
|------------|-------------------|--------|----------|--------|---------|--------|----------|------------|---------|--|--|
| Control    | 10                | 1.180± | 0. 044   | 0.412± | 0. 024  | 4.096± | 0. 185   | 1.788±     | 0. 042  |  |  |
| 640 ppm    | 10                | 1.177± | 0.067    | 0.398± | 0.031   | 4.219± | 0. 302   | 1.789±     | 0.060   |  |  |
| 1600 ppm   | 10                | 1.148± | 0.037    | 0.423± | 0.027   | 4.401± | 0.215*   | 1.778±     | 0. 024  |  |  |
| 4000 ppm   | 10                | 1.145± | 0.061    | 0.447± | 0.022*  | 4.899± | 0.259**  | $1.775\pm$ | 0. 047  |  |  |
| 7000 ppm   | 10                | 1.094± | 0.047**  | 0.495土 | 0.021** | 5.213土 | 0.169**  | 1.758土     | 0. 032  |  |  |
| 10000 ppm  | 10                | 1.079± | 0.042*** | 0.515± | 0.026** | 5.602± | 0. 180** | 1.726±     | 0.031** |  |  |

(HCL040)

BAIS 4

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### TABLE K 1

# ORGAN WEIGHT, RELATIVE: MALE

### ORGAN WEIGHT: RELATIVE (SUMMARY)

SURVIVAL ANIMALS ( 14W)

| Group Name | NO. of<br>Animals | Body Weight<br>(g)           | THYMUS            | ADRENALS          | TESTES            | HEART             | LUNGS             |  |
|------------|-------------------|------------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--|
| Control    | 10                | 309± 7                       | 0.079± 0.006      | 0.016 ± 0.001     | 1.014士 0.036      | 0.312± 0.014      | 0.316± 0.012      |  |
| 640 ppm    | 10                | $304 \pm 11$                 | $0.081 \pm 0.006$ | 0.017± 0.001      | 1. 039± 0. 029    | 0.310± 0.010      | 0.320± 0.013      |  |
|            |                   | $304 \pm 11$<br>$307 \pm 15$ | $0.074 \pm 0.005$ | $0.017 \pm 0.001$ | $1.062 \pm 0.047$ | 0.316± 0.010      | 0.315± 0.012      |  |
| 1600 ppm   | 10                |                              |                   | $0.017 \pm 0.001$ | 1. 120± 0. 099**  | $0.304 \pm 0.012$ | $0.317 \pm 0.012$ |  |
| 4000 ppm   | 10                | 299± 21                      | 0.074± 0.009      |                   |                   |                   |                   |  |
| 7000 ppm   | 10                | 276土 9**                     | 0.072± 0.005      | 0.018± 0.001**    | 1.203± 0.064**    | 0.317± 0.011      | 0.333± 0.009≭     |  |
| 10000 ppm  | 10                | 258± 9**                     | 0.071± 0.006*     | 0.019± 0.001**    | 1.278± 0.036₩*    | 0.320± 0.013      | 0.339± 0.012**    |  |

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

(HCL042)

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

PAGE : 2

| Group Name | NO. of<br>Animals | KIDNEYS           | SPLEEN                  | LIVER                   | BRAIN          | <br> |  |
|------------|-------------------|-------------------|-------------------------|-------------------------|----------------|------|--|
| ontrol     | 10                | 0.616± 0.020      | 0.196± 0.010            | 2. 420± 0. 082          | 0.620± 0.010   |      |  |
| i40 ppm    | 10                | 0.622± 0.023      | 0.199± 0.006            | 2.607± 0.123**          | 0.637± 0.020   | ~    |  |
| .600 ppm   | 10                | 0.641± 0.016      | 0.198± 0.008            | 2.872± 0.092**          | 0.636± 0.031   |      |  |
| 000 ppm    | 10                | 0.664± 0.025**    | 0.210± 0.009**          | 3.247± 0.106 <b>*</b> * | 0.642± 0.043   |      |  |
| 000 ppm    | 10                | 0.705± 0.019**    | 0.223± 0.007 <b>*</b> * | 3.424± 0.079 <b>*</b> * | 0.690± 0.019** |      |  |
| 0000 ppm   | 10                | 0.729± 0.039**    | 0.234± 0.011**          | 3.577± 0.122≉≉          | 0.730± 0.022₩  |      |  |
| Significa  | it difference ;   | * : P ≤ 0.05 ** : | $P \leq 0.01$           | Test                    | ; of Dunnett   |      |  |
| HCL042)    |                   |                   |                         |                         |                | <br> |  |

TABLE K 2

# ORGAN WEIGHT, RELATIVE: FEMALE

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

PAGE : 3

| Group Name | NO. of<br>Animals | Body Wei<br>(g    |      | THYMUS       | ADRENALS      | OVARIES      | HEART        | LUNGS          |   |
|------------|-------------------|-------------------|------|--------------|---------------|--------------|--------------|----------------|---|
| Control    | 10                | 176土              | 9    | 0.115± 0.014 | 0.032± 0.003  | 0.072± 0.007 | 0.370± 0.012 | 0.410± 0.020   |   |
| 40 ppm     | 10                | 173±              | 9    | 0.112± 0.013 | 0.033± 0.003  | 0.078± 0.029 | 0.373± 0.019 | 0.415± 0.027   |   |
| 600 ppm    | 10                | $167\pm$          | 9*   | 0.110± 0.008 | 0.034± 0.003  | 0.069± 0.007 | 0.373± 0.020 | 0.425± 0.020   |   |
| 1000 ppm   | 10                | 157土              | 7**  | 0.117± 0.012 | 0.036± 0.003* | 0.070± 0.011 | 0.387± 0.011 | 0.447± 0.022** |   |
| 000 ppm    | 10                | 152土              | 5**  | 0.116± 0.010 | 0.035± 0.003  | 0.072± 0.009 | 0.383± 0.013 | 0.439± 0.011*  |   |
| mqq 0000   | 10                | 150±              | 5**  | 0.108± 0.010 | 0.034± 0.003  | 0.067± 0.010 | 0.372± 0.017 | 0.440± 0.023*  |   |
| Significa  | nt difference ;   | * : $P \leq 0.05$ | ** : | P ≤ 0.01     | Tes           | t of Dunnett |              |                |   |
| (HCL042)   |                   |                   |      |              |               |              |              |                | I |

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

BRAIN Group Name NO. of KIDNEYS SPLEEN LIVER Animals 10 0.670 ± 0.016 0.234土 0.013 2.324± 0.067 1.016 ± 0.057 Control 1.034± 0.051 640 ppm 10 0.680土 0.034 0.230± 0.012 2.433 ± 0.090\* 0.253± 0.015\* 2.634± 0.099\*\*  $1.066 \pm 0.052$ 1600 ppm 10  $0.688 \pm 0.036$ 10 0.727± 0.017\*\* 3.112± 0.060\*\* 1.129± 0.050\*\* 4000 ppm 3.421± 0.066\*\* 1.154 - 0.040\*\* 7000 ppm 10 0.718± 0.019\*\* 0.325 ± 0.013\*\* 10000 ppm 10 0.722± 0.018\*\* 0.345± 0.021\*\* 3.749± 0.122\*\* 1.155± 0.028\*\*

\*\* : P ≦ 0.01

(HCL042)

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

Test of Dunnett

BAIS 4

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### TABLE L 1

### HISTOPATHOLOGICAL FINDINGS:

# NON-NEOPLASTIC LESIONS: MALE: ALL ANIMALS

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (O- 14W)

PAGE : 1

| Organ          | Findings                     | Group Name         Control           No. of Animals on Study         10           Grade         1         2         3         4           (%)         (%)         (%)         (%) | 640 µµm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%)         | 1600 ppm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 4000 µµm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|----------------|------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------|-----------------------------------------------------|-----------------------------------------------------|
| {Respiratory s | ystem}                       |                                                                                                                                                                                   | · · · · ·                                                  |                                                     |                                                     |
| nasal cavit    | mineralization               | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                            | <10> .<br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | <10><br>1 0 0 0<br>(10) (0) (0) (0)                 | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |
| lung           | accumulation of foamy cells  | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                            | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)                    | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |
| (Hematopoietic | system)                      |                                                                                                                                                                                   |                                                            |                                                     | н<br>С                                              |
| oone marrow    | erythropoiesis:increased     | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                            | <pre> &lt;10&gt;     0 0 0 0     ( 0) ( 0) ( 0) ( 0)</pre> | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |
| spleen         | deposit of hemosiderin       | <10><br>10 0 0 0<br>(100) ( 0) ( 0) ( 0)                                                                                                                                          | <10><br>10 0 0 0<br>(100) ( 0) ( 0) ( 0)                   | <10><br>10 0 0 0<br>(100) ( 0) ( 0) ( 0)            | <10><br>10 0 0 0<br>(100) ( 0) ( 0) ( 0)            |
|                | extramedullary hematopoiesis | 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)                      | 2 0 0 0<br>(20) (0) (0) (0)                         |
|                | engorgement of erythrocyte   | 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)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      |

(c) c: b / a \* 100 Significant difference; \*: P  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 14W)

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PAGE : 2

| Organ                  | Group N<br>No. of<br>Grade                                                                                                                                                 | Yame         7000 ppm           Animals on Study         10           1         2         3         4           (%)         (%)         (%)         (%) | 10000 ppm<br>10<br><u>i 2 3 4</u><br>(%) (%) (%) (%) |  |
|------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------|--|
| {Respiratory :         | system)                                                                                                                                                                    |                                                                                                                                                         |                                                      |  |
| nasal cavit            | mineralization                                                                                                                                                             | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                  | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |  |
| lung                   | accumulation of foamy cells                                                                                                                                                | ( 0) ( 0) ( 0) ( 0)<br>0 0 0 ( 0)<br><0 0 ( 0)                                                                                                          | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |  |
| {Hematopoieti          | c system)                                                                                                                                                                  |                                                                                                                                                         |                                                      |  |
| bone marrow            | erythropoiesis increased                                                                                                                                                   | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)                                                                                                                 | <10><br>4 0 0 0<br>(40) (0) (0) (0)                  |  |
| spleen                 | deposit of hemosiderin                                                                                                                                                     | <10><br>3 7 0 0 <b>**</b><br>( 30) ( 70) ( 0) ( 0)                                                                                                      | <10><br>0 10 0 0 ***<br>( 0) (100) ( 0) ( 0)         |  |
|                        | extramedullary hematopoiesis                                                                                                                                               | 7 0 0 0 <b>**</b><br>(70) ( 0) ( 0) ( 0)                                                                                                                | 10 0 0 0 **<br>(100) ( 0) ( 0) ( 0)                  |  |
|                        | engorgement of erythrocyte                                                                                                                                                 | 3 0 0 0<br>(30)(0)(0)(0)                                                                                                                                | 8 0 0 0 <b>**</b><br>(80) ( 0) ( 0) ( 0)             |  |
| <a>b<br/>b<br/>(c)</a> | 1 : Slight2 : Moderate3 : Marketa : Number of animals examined at the siteb : Number of animals with lesionc : b / a * 100ifference : $* : P \leq 0.05$ ** : $P \leq 0.01$ | ed 4 : Severe<br>Test of Chi Square                                                                                                                     |                                                      |  |

(IIPT150)

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| Organ                      | Findings                                                                                                                                                       | Group Name         Control           No. of Animals on Study         10           Grade         1         2         3         4           (%)         (%)         (%)         (%) | $\begin{array}{cccc} 640 & \text{ppm} \\ & 10 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | 1600 ppm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 4000 ppm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|----------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------|-----------------------------------------------------|
| {Circulator                | ry system}                                                                                                                                                     |                                                                                                                                                                                   |                                                                                                                        |                                                     |                                                     |
| heart                      | inflammatory cell nest                                                                                                                                         | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                            | <10><br>1 0 0 0<br>(10) (0) (0) (0)                                                                                    | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |
| {Digestive                 | system)                                                                                                                                                        |                                                                                                                                                                                   |                                                                                                                        |                                                     |                                                     |
| liver                      | hernialion                                                                                                                                                     | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                            | <10><br>2 0 0 0<br>(20) (0) (0) (0)                                                                                    | <10><br>2 0 0 0<br>(20) (0) (0) (0)                 | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)             |
|                            | hepatocellular hypertrophy: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 0<br>( 0) ( 0) ( 0) ( 0                       |
| {Urinary sy                | ystem)                                                                                                                                                         |                                                                                                                                                                                   |                                                                                                                        |                                                     |                                                     |
| k i dney                   | eosinophilic body                                                                                                                                              | <10><br>0 10 0 0<br>( 0) (100) ( 0) ( 0)                                                                                                                                          | <10><br>0 10 0 0<br>( 0) (100) ( 0) ( 0)                                                                               | <10><br>0 10 0 0 0<br>( 0) (100) ( 0) ( 0)          | <10><br>0 9 1 0<br>( 0) ( 90) ( 10) ( 0)            |
| {Endocrine                 | system}                                                                                                                                                        |                                                                                                                                                                                   |                                                                                                                        |                                                     |                                                     |
| thyroid                    | ultimobranchial body remanet                                                                                                                                   | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)                                                                                                                                           | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)                                                                                | <10><br>1 0 0 0<br>(10) (0) (0) (0)                 | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |
| Grade<br>< a ><br>b<br>(c) | <ul> <li>I: Slight 2: Moderate 3:</li> <li>a: Number of animals examined at the s</li> <li>b: Number of animals with lesion</li> <li>c: b / a * 100</li> </ul> | : Markod 1: Severe<br>site                                                                                                                                                        |                                                                                                                        |                                                     |                                                     |

(HPT150)

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 14W)

1

PAGE : 4

| Organ                                       | N                                                                                                                                               | roup Name         7000 ppm           p. of Animals on Study         10           crade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | • |   |   |  |
|---------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|---|---|---|--|
| {Circulatory                                | v svetom)                                                                                                                                       |                                                                                                                                                                                              |                                                       |   |   |   |  |
| heart                                       | inflammatory cell nest                                                                                                                          | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                       | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |   | · |   |  |
| {Digestive s                                | system)                                                                                                                                         | ·                                                                                                                                                                                            |                                                       |   |   |   |  |
| liver                                       | herniation                                                                                                                                      | <10><br>1 0 0 0<br>(10) (0) (0) (0)                                                                                                                                                          | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |   |   |   |  |
|                                             | hepatocellular hypertrophy:central                                                                                                              | 4 0 0 0<br>(40)(0)(0)(0)(0)                                                                                                                                                                  | 10 0 0 0 **<br>(100) ( 0) ( 0) ( 0)                   | , |   |   |  |
| {Urinary sys                                | sten)                                                                                                                                           |                                                                                                                                                                                              |                                                       |   |   |   |  |
| kidney                                      | eosinophilic body                                                                                                                               | <10><br>0 0 10 0 **<br>( 0) ( 0) (100) ( 0)                                                                                                                                                  | <10><br>0 0 10 0 <b>**</b><br>( 0) ( 0) (100) ( 0)    |   |   |   |  |
| {Endocrine s                                | system)                                                                                                                                         |                                                                                                                                                                                              |                                                       |   |   |   |  |
| thyroid                                     | ultimobranchial body remanet                                                                                                                    | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)                                                                                                                                                      | <10><br>1 0 0 0<br>(10) (0) (0) (0)                   |   |   |   |  |
| Grade<br>< a ><br>b<br>( c )<br>Significant | 1 : Slight2 : Moderate3 :a : Number of animals examined at the sitb : Number of animals with lesionc : b / a * 100difference ;* : P $\leq$ 0.05 |                                                                                                                                                                                              |                                                       |   |   | · |  |

(HPT150)

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 14W)

PAGE : 5

| Organ                                         | Group Nat<br>No. of Au<br>Grade<br>Findings                                                                                                                                 | ne Control<br>nimals on Study 10<br>(%) (%) (%) (%) | 640 µpm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 1600 ppm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 4000 ppm<br>10<br><u>1</u> <u>2</u> <u>3</u> <u>4</u><br>(%) (%) (%) (%) |
|-----------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------|----------------------------------------------------|-----------------------------------------------------|--------------------------------------------------------------------------|
| {Reproductive                                 | e system)                                                                                                                                                                   |                                                     |                                                    |                                                     |                                                                          |
| epididymis                                    | spermatogenic granuloma                                                                                                                                                     | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)             | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <10><br>1 0 0 0<br>(10) (0) (0) (0)                                      |
| (Special sens                                 | se organs/appendage)                                                                                                                                                        |                                                     |                                                    |                                                     |                                                                          |
| Harder gl                                     | lymphocytic infiltration                                                                                                                                                    | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)             | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)            | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)             | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   |
| Grade<br>< a ><br>b<br>( c )<br>Significant o | 1 : Slight2 : Moderate3 : Markeda : Number of animals examined at the siteb : Number of animals with lesionc : b / a * 100difference ; * : P $\leq 0.05$ ** : P $\leq 0.01$ | 4 : Severe<br>Test of Chi Square                    |                                                    |                                                     |                                                                          |

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 14W)

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| Organ                                       | Group Nam<br>No. of An<br>Grade<br>Findings                                                                                                                                                   | e 7000 ppm<br>imals on Study 10<br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |       |
|---------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|-------------------------------------------------------|-------|
| {Reproductiv                                |                                                                                                                                                                                               |                                                    |                                                       |       |
| epididymis                                  | spermatogenic granuloma                                                                                                                                                                       | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)             | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |       |
| {Special sen                                | se organs/appendage)                                                                                                                                                                          |                                                    |                                                       |       |
| Harder gl                                   | lymphocytic infiltration                                                                                                                                                                      | <10><br>2 0 0 0<br>(20) (0) (0) (0)                | <10><br>1 0 0 0<br>(10) (0) (0) (0)                   |       |
| Grade<br>< a ><br>b<br>( c )<br>Significant | 1 : Slight 2 : Moderate 3 : Marked<br>a : Number of animals examined at the site<br>b : Number of animals with lesion<br>c : b / a * 100<br>difference ; * : P $\leq 0.05$ ** : P $\leq 0.01$ | 4 : Severe<br>Test of Chi Square                   |                                                       |       |
|                                             |                                                                                                                                                                                               | -                                                  |                                                       | PATCA |

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### TABLE L 2

### HISTOPATHOLOGICAL FINDINGS:

# NON-NEOPLASTIC LESIONS: FEMALE: ALL ANIMALS

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 14W)

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| Orgati                       | Ν                                                                                                                                                                                | roup Name Control<br>o. of Animals on Study 10<br>rade <u>1 2 3 4</u><br>(%) (%) (%) (%) | 640 ppm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 1600 ppm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 4000 ppm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|----------------------------------------------------|-----------------------------------------------------|-----------------------------------------------------|
|                              |                                                                                                                                                                                  | · · · · · · · · · · · · · · · · · · ·                                                    |                                                    |                                                     |                                                     |
| (Hematopoieti                | c system}                                                                                                                                                                        |                                                                                          |                                                    |                                                     |                                                     |
| bone marrow                  | granulation                                                                                                                                                                      | <10> ~<br>3 0 0 0<br>( 30) ( 0) ( 0) ( 0)                                                | <10><br>3 1 0 0<br>( 30) ( 10) ( 0) ( 0)           | <10><br>2 1 0 0<br>(20) (10) (0) (0)                | <10><br>2 0 0 0<br>(20) (0) (0) (0)                 |
|                              | myelofibrosis                                                                                                                                                                    | 0 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)                      |
|                              | erythropoiesis:increased                                                                                                                                                         | , 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)                      |
| spleen                       | deposit of hemosiderin                                                                                                                                                           | <10><br>10 0 0 0<br>(100) ( 0) ( 0) ( 0)                                                 | <10><br>10 0 0 0<br>(100) ( 0) ( 0) ( 0)           | <10><br>10 0 0 0<br>(100) ( 0) ( 0) ( 0)            | <10><br>10 0 0 0<br>(100) ( 0) ( 0) ( 0)            |
|                              | extramedullary hematopoiesis                                                                                                                                                     | 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)                      | 1 0 0 0<br>(10) (0) (0) (0)                         |
|                              | engorgement of erythrocyte                                                                                                                                                       | . ( 0) ( 0) ( 0) ( 0)                                                                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 3 0 0 0<br>(30) (0) (0) (0)                         |
| Digestive sy                 | rstem)                                                                                                                                                                           |                                                                                          |                                                    |                                                     |                                                     |
| liver                        | herniation                                                                                                                                                                       | <10><br>1 0 0 0<br>(10) (0) (0) (0)                                                      | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)             | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)             | <10><br>2 0 0 0<br>( 20) ( 0) ( 0) ( 0)             |
| Grade<br>< a ><br>b<br>( c ) | 1 : Slight 2 : Moderate 3 :<br>a : Number of animals examined at the sit<br>b : Number of animals with lesion<br>c : b / a * 100<br>lifference ; * : $P \leq 0.05$ ** : $P \leq$ |                                                                                          |                                                    |                                                     |                                                     |
| Significant C                |                                                                                                                                                                                  |                                                                                          |                                                    |                                                     |                                                     |

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#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 14W)

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| Organ          | Findings                     | Group Name         7000 ppm           No. of Animals on Study         10           Grade         1         2         3         4           (%)         (%)         (%)         (%) | 10000 ppm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |  |
|----------------|------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------|--|
|                |                              |                                                                                                                                                                                    |                                                      |  |
| {Hematopoietic | : system)                    |                                                                                                                                                                                    |                                                      |  |
| bone marrow    | granulation                  | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                             | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)              |  |
|                | myelofibrosis                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |  |
|                | erythropoiesis:increased     | L 0 0 0<br>(10) (0) (0) (0)                                                                                                                                                        | 4 0 0 0<br>(40)(0)(0)(0)                             |  |
| spleen         | deposit of hemosiderin       | <10><br>I 9 0 0 ***<br>( 10) ( 90) ( 0) ( 0)                                                                                                                                       | <10><br>2 8 0 0 **<br>( 20) ( 80) ( 0) ( 0)          |  |
|                | extramedullary hematopoiesis | 10 0 0 ***<br>(100) ( 0) ( 0) ( 0)                                                                                                                                                 | 10 0 0 0 **<br>(100) ( 0) ( 0) ( 0)                  |  |
|                | engorgement of erythrocyte   | 10 0 0 0 **<br>(100) ( 0) ( 0) ( 0)                                                                                                                                                | 10 0 0 0 **<br>(100) ( 0) ( 0) ( 0)                  |  |
| Digestive sys  | tem)                         |                                                                                                                                                                                    |                                                      |  |
| liver          | herniation                   | <10><br>i 0 0 0<br>( 10) ( 0) ( 0) ( 0)                                                                                                                                            | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)              |  |

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

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 14W)

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| Organ                                       |                                                                                                                                                                                 | р Name Control<br>of Animals on Study 10<br>le <u>I 2 3 4</u><br>(%) (%) (%) (%) | 640 ppm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 1600 ppm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 4000 ppm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|---------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|----------------------------------------------------|-----------------------------------------------------|-----------------------------------------------------|
|                                             |                                                                                                                                                                                 |                                                                                  |                                                    |                                                     | ·                                                   |
| {Digestive s                                | ystem}                                                                                                                                                                          |                                                                                  |                                                    |                                                     |                                                     |
| liver                                       | inflammatory cell nest                                                                                                                                                          | <10><br>1 0 0 0<br>(10) (0) (0) (0)                                              | <10><br>1 0 0 0<br>(10) (0) (0) (0)                | <10><br>1 0 0 0<br>(10) (0) (0) (0)                 | <10><br>1 0 0 0<br>(10) (0) (0) (0)                 |
|                                             | hepatocellular hypertrophy: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)                          |
| {Urinary sys                                | tem)                                                                                                                                                                            |                                                                                  |                                                    |                                                     |                                                     |
| kidney                                      | mineralization:cortico-medullary junction                                                                                                                                       | <10><br>2 0 0 0<br>(20) (0) (0) (0)                                              | <10><br>2 0 0 0<br>( 20) ( 0) ( 0) ( 0)            | <10><br>5 0 0 0<br>(50) ( 0) ( 0) ( 0)              | <10><br>2 0 0 0<br>( 20) ( 0) ( 0) ( 0)             |
|                                             | mineralization:papilla                                                                                                                                                          | 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)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      |
|                                             | deposit of brown pigment:proximal tubule                                                                                                                                        | 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)                      | 10 0 0 0 **<br>(100) ( 0) ( 0) ( 0)                 |
| {Endocrine s                                | ystem)                                                                                                                                                                          |                                                                                  |                                                    |                                                     |                                                     |
| pituitary                                   | Rathke pouch                                                                                                                                                                    | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                           | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)             | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |
| Grade<br>< a ><br>b<br>( c )<br>Significant | 1: Slight 2: Moderate 3: Ma<br>a: Number of animals examined at the site<br>b: Number of animals with lesion<br>c: b / a * 100<br>difference; $*: P \leq 0.05  **: P \leq 0.05$ |                                                                                  |                                                    |                                                     |                                                     |

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#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (O- 14W)

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| Organ                                         |                                                                                                                                                                                            | of Animals on Study | 7000 ppm<br>10<br><u>2 3</u><br>(%) (%) | 4              | 10000 ppm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | <br> |
|-----------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|-----------------------------------------|----------------|------------------------------------------------------|------|
| {Digestive sy                                 | ystem)                                                                                                                                                                                     |                     |                                         |                |                                                      |      |
| liver                                         | inflammatory cell nest                                                                                                                                                                     | 1<br>( 10)          | <10><br>0 0<br>( 0) ( 0)                |                | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |      |
|                                               | hepatocellular hypertrophy:central                                                                                                                                                         | 7<br>(70)           | 0 0<br>(0)(0)                           | 0 **<br>) ( 0) | 10 0 0 **<br>(100) ( 0) ( 0) ( 0)                    |      |
| {Urinary syst                                 | tem)                                                                                                                                                                                       |                     |                                         |                |                                                      |      |
| kidney                                        | mineralization:cortico-medullary junction                                                                                                                                                  | 3<br>(30)           | <10><br>0 0<br>( 0) ( 0)                | 0)(0)          | <10><br>1 0 0 0<br>(10) (0) (0) (0)                  |      |
|                                               | mineralization:papilla                                                                                                                                                                     | 0<br>( 0)           | 0 0<br>( 0) ( 0)                        | 0<br>) ( 0)    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |      |
|                                               | deposit of brown pigment:proximal tubule                                                                                                                                                   | 0<br>( 0)           | 10 0<br>(100) ( 0)                      | 0 **<br>) ( 0) | 0 10 0 0 **<br>( 0) (100) ( 0) ( 0)                  |      |
| {Endocrine s                                  | ystem)                                                                                                                                                                                     |                     |                                         |                |                                                      |      |
| pituitary                                     | Rathke pouch                                                                                                                                                                               | 0<br>( 0)           | <10><br>0 0<br>( 0) ( 0)                |                | <10><br>1 0 0 0<br>(10) ( 0) ( 0) ( 0)               |      |
| Grade<br>< a ><br>b<br>( c )<br>Significant ( | 1 : Slight 2 : Moderate 3 : Mata<br>a : Number of animals examined at the site<br>b : Number of animals with lesion<br>c : b / a * 100<br>difference ; * : $P \leq 0.05$ ** : $P \leq 0.0$ |                     |                                         |                |                                                      |      |

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#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 14W)

| SEX                    | : FEMALE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                   |                                                    |                                                      | PAGE                                                |
|------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|----------------------------------------------------|------------------------------------------------------|-----------------------------------------------------|
| .gan                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | np Name Control<br>of Animals on Study 10<br>le <u>I 2 3 4</u><br>(%) (%) (%) (%) | 640 ppm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 4000 µpm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| Endocrine              | system)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                   |                                                    |                                                      |                                                     |
| hyroid                 | ultimobranchial body remanet                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | <10><br>1 0 0 0<br>(10) (0) (0) (0)                                               | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)             | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               | <10><br>1 0 0 0<br>(10) (0) (0) (0)                 |
| Reproducti             | ve system)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                   |                                                    |                                                      |                                                     |
| vary                   | cyst                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                            | <10><br>i 0 0 0<br>(10) (0) (0) (0)                | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |
| Special se             | nse organs/appendage)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                   |                                                    |                                                      |                                                     |
| arder gl               | lymphocytic infiltration                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | <10><br>5 0 0 0<br>(50) (0) (0) (0)                                               | <10><br>5 0 0 0<br>(50) (0) (0) (0)                | <10><br>3 1 0 0<br>( 30) ( 10) ( 0) ( 0)             | 3 0 0 0<br>(30) (0) (0) (0)                         |
| rade<br>a ≻<br>b<br>c) | 1: Slight 2: Moderate 3: Mathematical Mathematical Mathematical Action and the site b: Number of animals with lesion c: b / a $\times$ 100 definition for the site of | •                                                                                 |                                                    |                                                      |                                                     |

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

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#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (O- 14W)

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| 0rgan                                       | Findings                                                                                                                                      | Group Name         7000 ppm           No. of Animals on Study         10           Grade         1         2         3         4           (%)         (%)         (%)         (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$                 | · |
|---------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------|---|
| {Endocrine :                                | system)                                                                                                                                       |                                                                                                                                                                                    |                                                                       |   |
| thyroid                                     | ultimobranchial body remanet                                                                                                                  | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                             | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)                               |   |
| {Reproducti                                 | ve system)                                                                                                                                    |                                                                                                                                                                                    |                                                                       |   |
| ovary                                       | cyst                                                                                                                                          | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                             | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                |   |
| {Special ser                                | nse organs/appendage)                                                                                                                         |                                                                                                                                                                                    |                                                                       |   |
| flarder gl                                  | lymphocytic infiltration                                                                                                                      | <10><br>3 0 0 0<br>( 30) ( 0) ( 0) ( 0)                                                                                                                                            | <pre> &lt;10&gt; </pre> <pre> 4 0 0 0 ( 40) ( 0) ( 0) ( 0) ( 0)</pre> |   |
| Grade<br>< a ><br>b<br>( c )<br>Significant | 1 : Slight2 : Moderatea : Number of animals examined at thb : Number of animals with lesionc : b / a * 100difference ; * : $P \leq 0.05$ ** : |                                                                                                                                                                                    |                                                                       |   |

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