グリシドールのラットを用いた 吸入による 13 週間毒性試験報告書

試験番号:0316

APPENDIX

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APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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STUDY NO. : 0316 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 13

SEX : MALE

PAGE: 1

Clinical sign	Group Name	Admini	stration We	ek-day										
		1-7 1	2-7 1	3-7 1	4-7 1	5-7	6-7 1	7-7	8-7	9-7 1	10-7	11-7	12-7	13-7 1
									-	-				•
ЕЛТН	maa0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	80ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	160ppm	1	3	3	4	4	4	4	5	5	5	5	5	5
UNCHBACK POSITION	0ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10ppm	0	0	0	0	0	0	0	0	0	0	0	Ő	0
	20ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	80ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	160ppm	0	0	0	0	0	0	1	0	0	0	0	0	0
ILOERECTION	0ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10ppm	0	0	0	0	0	0	0	0	0	0	Ō	Ő	õ
	20ppm	0	0	0	0	0	0	0	0	Ö	Ö	ů i	Ő	Õ
	40ppm	0	0	0	0	Ó	0	0	Ō	Õ	õ	Ő	Ő	õ
	80ppm	0	0	0	0	0	0	0	0	0	0	Ō	Ő	Ō
	160ppm	0	0	0	0	0	0	1	0	0	0	0	Ő	Ő

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APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

STUDY NO. : 0316 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : FEMALE

PAGE	:	2
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linical sign	Group Name	Adminis	stration W	əək-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	
		1	1	1	1	1	1	1	1	1	1	1	1	1	
1 A TT I J	0	0	0	0	0	٥	0	٥	0	0	0	0	0	0	
EATH	0ppm 10ppm	0 0	-	0	0	0	0	0	0	0	0	0	0	0	
	10ppm	0	0	0	0	0	0	0 0	0	0	0	0	0	0	
	20ppm	0	0	0	0	0	0	0	0	•	-	0	0	•	
	40ppm	0	0	0	0	-	0		0	0	0	•	v	0	
	80ppm	0	1	0 3	-	0 5	0 5	0 7	8	0	0	0	0	0	
	160ppm	U	1	3	4	Ð	Ð	7	8	8	8	8	8	8	
NCHBACK POSITION	0ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	10ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	20ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	40ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	80ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	160ppm	0	0	4	3	2	2	1	0	0	0	0	0	0	
LOERECTION	0ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	10ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	20ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	40ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	80ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	160ppm	0	0	0	1	0	0	1	2	2	0	0	0	0	
OPHTHALMOS	0ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	10ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	20ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	40ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	mqq08	0	1	1	0	0	0	0	0	0	0	0	0	0	
	160ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
E OPACITY	maq0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	10ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	20ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	
	40ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	80ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	160ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
TARACT	mqq0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	10ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	20ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	
	40ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	80ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	160ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	

STUDY NO. : 0316 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 13

SEX : FEMALE

PAGE : 3

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Clinical sign	Group Name	Admini	stration We	ek-day											
		1 -7	2-7 1	3-7	4-7 1	5-7 1	6-7 1	7-7	8-7 1	9-7	10-7	11-7	12-7	13-7	
		•	-		+	.	*	-					1		
ABNORMAL RESPIRA.SOUND	0ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	10ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	20ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	40ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	80ppm	0	0	0	0	0	0	0	0	0	0	ů 0	ů	Ő	
	160ppm	1	0	0	0	0	0	0	0	Ó	0	0	0	0	

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ALL ANIMALS

CLINICAL OBSERVATION (SUMMARY)

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APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, RAT : MALE

BODY WEIGHT CHANGES ALL ANIMALS

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STUDY NO.: 0316 ANIMAL : RAT F344/DuCrj UNIT : g REPORT TYPE : A1 13 SEX : MALE

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PAGE: 1

Name	Admini	stration	week-day											
	0-0		1-7		2-7		3-7	· · · · · · · · · · · · · · · · · · ·	4-7		5-7		6-7	
0ppm	107±	4	135±	7	163±	8	183±	9	202±	9	219±	10	$231\pm$	11
10ppm	107±	4	$134\pm$	6	162±	7	182±	8	199±	9	$215\pm$	8	$226\pm$	8
20ppm	107±	4	$133\pm$	5	161±	8	180±	10	197±	12	$211\pm$	12	222±	12
40ppm	107±	4	130±	6	158±	8	178±	9	195±	10	210±	11	220±	12
80ppm	107±	4	$125\pm$	5**	150±	7**	170±	10*	187±	12**	$201\pm$	13**	213±	14**
160ppm	107±	4	100±	7**	99±	12**	106±	8**	113±	10**	114±	14**	$122\pm$	18**
ignificant differenc	ce; *:P≦(0.05	** : P ≦ 0.0	1			Test of Du	unnett						
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(SUMMARY)

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BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS ~_____/

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STUDY NO. : 0316 ANIMAL : RAT F344/DuCrj UNIT : g REPORT TYPE : A1 13 SEX : MALE

.p Name	Admini	istration	week-day											
	7-7		8-7		9–7		10-7		11-7		12-7		13-7	
Maado	243±	13	$255\pm$	14	266±	14	274±	17	$281\pm$	17	289±	17	$294\pm$	18
10ppm	236±	8	247±	8	257±	8	264±	8	271±	10	276±	10	280±	12
20ppm	$231\pm$	14	$240\pm$	14	251±	14	260±	15	$265\pm$	15*	270±	16*	274±	16*
40ppm	229±	12	240±	12	249±	14*	255±	13*	262±	14*	267±	15**	274±	16*
80ppm	219±	13**	227±	15**	$235\pm$	13**	242±	14**	246±	13**	$251\pm$	13**	255±	12**
160ppm	122±	25**	$134\pm$	13**	$137\pm$	11**	$141\pm$	14**	$141\pm$	13**	142±	16**	142±	17**
Significant difference	; *:P≦(** : P ≤ 0.(Test of Du							

(HAN260)

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PAGE: 2

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

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STUDY NO. : 0316 ANIMAL : RAT F344/DuCrj UNIT : g REPORT TYPE : A1 13 SEX : FEMALE

PAGE : 3

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1-7 112 ± 3 110 ± 3 108 ± 3 109 ± 4 $104\pm 3**$	123± 121± 122±	4 4 4	130± 128±	3 6 4 5	4-7 142± 138± 133± 134±	5 7 6* 5	5-7 149± 143± 139± 137±	5 6 6**	6-7 153± 147± 142± 139±	5 7 6**
110± 3 108± 3 109± 4	$123 \pm$ $121 \pm$ $122 \pm$	4 4 4	130± 128±	6 4	$138\pm$ $133\pm$	7 6*	143± 139±	6 6**	147± 142±	7 6**
108± 3 109± 4	$121\pm$ $122\pm$	4 4	128±	4	133±	6*	139±	6**	142±	6**
109± 4	122±	4								
			128±	5	$134\pm$	5	$137\pm$	6**	139±	6**
104+ 3**	116+									
	110.1	4**	$124\pm$	4**	129±	4**	$134\pm$	6**	$138\pm$	6**
83± 6**	78±	9**	81± 3	11**	83±	15**	88±	8**	88±	14**
: P ≤ 0.01			Test of Durn	nett						
	P ≦ 0.01	P ≤ 0.01	$P \leq 0.01$	$P \leq 0.01$ Test of Dur	P ≦ 0.01 Test of Dunnett	P ≤ 0.01 Test of Dunnett	P ≤ 0.01 Test of Dunnett	$P \leq 0.01$ Test of Dunnett	P ≤ 0.01 Test of Dunnett	$P \leq 0.01$ Test of Dunnett

BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

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STUDY NO. : 0316 ANIMAL : RAT F344/DuCrj UNIT : g REPORT TYPE : A1 13 SEX : FEMALE

PAGE: 4

Name		istration								·				
	7-7		8-7		9–7		10-7		11-7		12-7		13-7	
0ppm	156±	6	162±	6	164±	7	169±	7	173±	8	175±	8	179±	8
10ppm	$150\pm$	7	153±	8*	156±	9	160±	10	162±	9*	165±	9*	166±	10*
20ppm	147±	6*	150±	6**	$152\pm$	8**	155±	7**	$157\pm$	8**	159±	7**	162±	9**
40ppm	143±	7**	$145\pm$	6**	149±	7**	152±	7**	153±	8**	155±	8**	156±	8**
80ppm	141±	7**	142±	7**	148±	9**	148±	8**	$152\pm$	7**	$152\pm$	8**	153±	9**
160ppm	91±	18**	99±	1 ?	101±	3 ?	105±	1 ?	99±	0 ?	104±	1 ?	100±	1 ?
					10, 1				,					
Significant differenc	xe; ∗:P≦	0.05 ;	** : P ≦ 0.0)1			Test of Du	unnett						

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

(HAN260)

APPENDIX C 1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

STUDY NO.: 0316 ANIMAL : RAT F344/DuCrj UNIT : g REPORT TYPE : A1 13 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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PAGE: 1

o Name	Administration 1-7(6)	week-day(effective) 2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
0ppm	13.2± 1.1	14.3± 0.9	15.4± 1.2	16.2± 1.4	15.8± 0.9	15.6± 1.2	16.0± 1.2
10ppm	13.0± 0.6	14.0± 0.7	15.3± 0.5	15.4± 0.7	15.0± 0.8	14.7± 0.7	15.3± 1.3
20ppm	13.2± 1.0	14.3 ± 1.2	15.8± 1.7	16.0± 1.5	15.1± 1.3	15.0± 1.4	15.3± 1.7
40ppm	12.1± 0.8*	13.6± 0.9	14.7± 1.2	15.5± 1.3	14.9± 0.9	14.8± 1.1	14.7± 1.2
80ppm	11.2± 0.9**	13.0± 0.7*	14.7 ± 1.3	15.0± 1.0	14.6± 0.7*	15.3 ± 1.5	14.2± 1.0*
160ppm	6.3± 1.0**	7.4± 1.6**	8.4± 0.5**	9.6± 1.6**	8.6± 1.4**	9.0± 1.3**	8.6± 1.8**
Significant differen	ce; *:P≦0.05	** : P ≦ 0.01		Test of Dunnett			
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STUDY NO.: 0316 ANIMAL : RAT F344/DuCrj UNIT : g REPORT TYPE : A1 13 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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PAGE : 2

Name	Administration	week-day(effective)					
	8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)	
Oppm	15.3± 0.9	15.5± 1.1	16.0± 1.0	15.3± 0.8	15.5± 0.9	15.2± 1.1	
10ppm	14.4± 0.4	14.5± 0.6	14.4± 0.7**	14.6± 0.6	14.2± 0.6*	14.1± 0.8	
20ppm	14.5± 0.8	14.4± 0.9	14.3± 1.0**	14.5± 0.7	14.2± 0.9*	14.1± 1.2	
40ppm	14.6± 0.9	14.6± 1.4	14.2± 1.0**	14.2± 1.2*	14.1± 1.0**	14.5± 1.1	
80ppm	14.6± 1.1	14.2± 0.7*	14.1± 1.1**	13.9± 1.2**	13.9± 0.8**	13.6± 0.8**	
160ppm	9.2± 0.7**	9.0± 0.3**	9.8± 1.2**	9.3 土 0.5**	9.7± 1.2**	9.3± 1.1**	
ignificant difference	; *:P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett			

APPENDIX C 2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

STUDY NO. : 0316 ANIMAL : RAT F344/DuCrj UNIT : g REPORT TYPE : A1 13 SEX : FEMALE

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FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE : 3

up Name	Administration 1-7(6)	week-day(effective) 2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Oppm	11.3± 0.4	11.4± 0.7	11.4± 0.5	11.5± 0.7	11.2± 0.6	10.9± 0.8	10.8± 0.7
10ppm	10.3± 0.5	10.8± 0.8	10.9± 0.9	11.1± 0.7	10.5± 0.8	10.1± 0.7	10.0± 0.9
20ppm	10.9± 0.8	11.0± 0.5	10.9± 0.7	10.8± 0.6	10.3± 0.5*	10.2± 0.7	10.2± 0.6
40ppm	10.3± 0.7	10.8± 0.4	10.7± 0.6	10.9± 1.0	10.2± 1.0**	9.8± 0.7**	9.9± 0.3*
80ppm	9.0± 1.0**	10.3± 0.5*	10.7± 0.4	10.7± 0.5	10.2± 0.6*	10.2± 0.7	9.6± 0.6**
160ppm	4.8± 1.4**	5.8± 1.4**	6.6± 1.5**	7.1± 1.6**	6.7± 0.5**	7.0± 0.8**	6.3± 1.9**
Significant difference ;	*:P≦0.05	** : P ≦ 0.01		Test of Dunnett			

STUDY NO.: 0316 ANIMAL : RAT 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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o Name	Administration 8-7(7)	week-day(effective) 9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
0ppm	10.6± 0.8	10.9± 0.8	10.6± 0.7	11.0± 0.8	10.8± 0.7	11.3± 0.8
10ppm	9.7± 0.9*	10.1± 0.9	9.6± 1.0*	9.9± 0.7**	10.2± 0.5	9.8± 0.7**
20ppm	9.9± 0.8	9.9± 1.2	9.4± 0.5**	9.4± 0.4**	9.8± 0.5**	9.9± 0.9**
40ppm	9.4± 0.7**	9.8± 0.8	9.4± 0.6**	9.1± 0.7**	9.5± 0.8**	9.4± 0.7**
80ppm	9.7± 0.8*	9.9± 0.9	9.3± 0.7**	9.4± 0.9**	9.4± 0.7**	9.5± 1.1**
160ppm	6.6± 0.6 ?	6.7± 0.4 ?	7.5± 0.3 ?	6.7± 0.0 ?	7.6± 0.4 ?	6.6± 0.1 ?

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

(HAN260)

APPENDIX D 1

HEMATOLOGY : SUMMARY, RAT : MALE

STUDY NO. : 0316 ANIMAL : RAT F34 MEASURE. TIME : 1	4/DuCrj	HEMATOLOGY (SUMMARY) ALL ANIMALS (14W)
SEX : FEMALE	REPORT TYPE : A1	

PAGE :	4
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roup Name	NO. of Animals	RED BL 1 0⁵∕	OOD CELL με	HEMOGLO g ⁄d2		HEMATOO %	CRIT	MCV f Q		MCH Pg		MCHC g / dl		PLATELE 1 0 ³ /µ	
0 Dodu	10	8.61±	0.28	16.4±	0.2	45.9±	1.5	53.3±	1.0	19.0±	0.6	35.7±	1.0	743±	46
10ppm	10	8.51±	0.27	16.2±	0.2	45.0±	1.5	52.9±	0.7	19.1±	0.6	36.1±	1.1	758±	46
20ppm	10	8.61±	0.26	16.2±	0.4	45.8±	1.5	53.1±	0.6	18.8±	0.2	35.4±	0.5	774±	37
40ppm	10	8.27±	0.46	15.8±	0.2**	43.9±	2.3	53.1±	0.9	19.2±	1.4	36.1±	2.4	773±	58
mqq08	10	7.76±	0.43**	15.1±	0.4**	42.1±	2.4**	54.2±	1.0	19.5±	1.1	35.9±	2.1	794±	79
160ppm	2	7.83±	0.47 ?	$14.7\pm$	1.1 ?	43.2±	3.7 ?	55.2±	1.3 ?	18.8±	0.3 ?	34.1±	0.3 ?	771±	42 ?

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

(HCL070)

STUDY NO. : 0316 ANIMAL : RAT F344/DuCrj MEASURE. TIME : 1 SEX : FEMALE REPORT TYPE : A1 HEMATOLOGY (SUMMARY) ALL ANIMALS (14W)

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o Name	NO. of Animals	RETICULO ‰	OCYTE	PROTHRO sec	OMBIN TIME	APTT sec	
0ppm	10	21±	7	11.5±	0.5	18.2±	1.7
10ppm	10	23±	3	11.9±	0.5	18.4±	0.7
20ppm	10	27±	4*	11.7±	0.5	18.4±	0.6
40ppm	10	24±	4	11.6±	0.4	18.3±	0.7
80ppm	10	$29\pm$	5**	11.7±	0.4	18.4±	0.6
160ppm	2	24±	2 ?	12.1±	0.0 ?	19.1±	1.3 ?

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

(HCL070)

BAIS 3

PAGE: 5

STUDY NO. : 0316 ANIMAL : RAT F344/DuCrj MEASURE. TIME : 1 SEX : FEMALE REPORT TYPE : A1

ALL ANIMALS (14W)

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Group Name NO. of WBC Differential WBC (%) Animals 1 0³/μl N-BAND EOSINO BASO LYMPHO N-SEG MONO 0ppm 10 3.31± 1.22 0± 0  $22\pm$ 6  $2\pm$ 0±  $4\pm$ 1 0 2  $72\pm$ 10ppm 10 3.75± 1.39 0± 0  $22\pm$ 6  $1\pm$ 0±  $4\pm$ 1 0 2  $72\pm$ 20ppm 10 4.09± 1.76 0± 0  $24\pm$ 8  $1\pm$ 0± 0  $4\pm$ 1 2  $71\pm$ 40ppm 10 0 3.14± 0.43  $0\pm$  $25\pm$ 5  $1\pm$ 1 0± 0  $3\pm$ 1  $71\pm$ 

6

23 ?

 $1\pm$ 

 $1\pm$ 

1

1 ?

Test of Dunnett

0±

0±

0

0 ?

 $4\pm$ 

 $2\pm$ 

,

1

1 ?

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

0土

0±

\*\* : P ≦ 0.01

0

0 ?

 $26\pm$ 

 $43\pm$ 

3.55± 0.53

4.20± 0.73 ?

(HCL070)

80ppm

160ppm

10

2

Significant difference ;  $*: P \leq 0.05$ 

BAIS 3

| PAGE | : | 6 |
|------|---|---|
|------|---|---|

0

0

0

0

0

0 ?

OTHERS

0±

 $0\pm$ 

0±

 $0\pm$ 

0±

 $0\pm$ 

6

5

7

5

5

23 ?

 $69\pm$ 

 $55\pm$ 

HEMATOLOGY (SUMMARY)

APPENDIX D 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

STUDY NO. : 0316 ANIMAL : RAT F344/DuGrj MEASURE. TIME : 1 SEX : MALE 007 700

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

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| ACFORT 1          | FYPE : A1                             |                                                                                                                 |                                                                                                                                    |                                                                                                                                                                                                              |                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                               | PAGE :                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|-------------------|---------------------------------------|-----------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| NO. of<br>Animals |                                       |                                                                                                                 |                                                                                                                                    |                                                                                                                                                                                                              | HEMATOC<br>%                                                                                                                                                                                                                               | RIT                                                                                                                                                                                                                                                                                 | MCV<br>f Q                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                       | MCH<br>Pg                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | MCHC<br>g / dl                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| 10                | 9.32±                                 | 0.36                                                                                                            | 16.4±                                                                                                                              | 0.3                                                                                                                                                                                                          | 46.8±                                                                                                                                                                                                                                      | 2.0                                                                                                                                                                                                                                                                                 | 50.2±                                                                                                                                                                                                                                                                                              | 0.5                                                                                                                                                                                                                                                                                                                                                                                                   | 17.6±                                                                                                                                                                                                                                                                                                                                                                       | 0.7                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 35.2±                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 1.7                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 711±                                                                          | 42                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| 10                | 9.21±                                 | 0.40                                                                                                            | 16.3±                                                                                                                              | 0.3                                                                                                                                                                                                          | 46.1±                                                                                                                                                                                                                                      | 2.0                                                                                                                                                                                                                                                                                 | 50.0±                                                                                                                                                                                                                                                                                              | 0.7                                                                                                                                                                                                                                                                                                                                                                                                   | 17.8±                                                                                                                                                                                                                                                                                                                                                                       | 0.9                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 35.6±                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 1.6                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | $697\pm$                                                                      | 50                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| 10                | 9.34±                                 | 0.26                                                                                                            | 16.3±                                                                                                                              | 0.2                                                                                                                                                                                                          | 47.0±                                                                                                                                                                                                                                      | 1.6                                                                                                                                                                                                                                                                                 | 50.3±                                                                                                                                                                                                                                                                                              | 0.7                                                                                                                                                                                                                                                                                                                                                                                                   | 17.5±                                                                                                                                                                                                                                                                                                                                                                       | 0.5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 34.7±                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 1.2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 708±                                                                          | 45                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| 10                | 9.38±                                 | 0.28                                                                                                            | 16.1±                                                                                                                              | 0.2                                                                                                                                                                                                          | 47.1±                                                                                                                                                                                                                                      | 1.6                                                                                                                                                                                                                                                                                 | 50.2±                                                                                                                                                                                                                                                                                              | 0.8                                                                                                                                                                                                                                                                                                                                                                                                   | 17.2±                                                                                                                                                                                                                                                                                                                                                                       | 0.5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 34.3±                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 0.9                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 710±                                                                          | 46                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| 10                | 8.89±                                 | 0.34*                                                                                                           | 15.6±                                                                                                                              | 0.3**                                                                                                                                                                                                        | 44.8±                                                                                                                                                                                                                                      | 1.7                                                                                                                                                                                                                                                                                 | 50.4±                                                                                                                                                                                                                                                                                              | 0.9                                                                                                                                                                                                                                                                                                                                                                                                   | 17.6±                                                                                                                                                                                                                                                                                                                                                                       | 0.8                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 34.9±                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 1.3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 769±                                                                          | 41                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| 5                 | 8.08±                                 | 0.52**                                                                                                          | 14.6±                                                                                                                              | 0.7**                                                                                                                                                                                                        | 43.2±                                                                                                                                                                                                                                      | 3.6**                                                                                                                                                                                                                                                                               | 53.5±                                                                                                                                                                                                                                                                                              | 1.3**                                                                                                                                                                                                                                                                                                                                                                                                 | 18.0±                                                                                                                                                                                                                                                                                                                                                                       | 0.3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 33.8±                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 1.3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 712±                                                                          | 86                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|                   | Animals<br>10<br>10<br>10<br>10<br>10 | Animals     106/       10     9.32±       10     9.21±       10     9.34±       10     9.38±       10     8.89± | Animals $1 0^6 / \mu l$ 10 $9.32 \pm$ $0.36$ 10 $9.21 \pm$ $0.40$ 10 $9.34 \pm$ $0.26$ 10 $9.38 \pm$ $0.28$ 10 $8.89 \pm$ $0.34 *$ | Animals       1 0 <sup>6</sup> /µl       g/dl         10 $9.32\pm$ $0.36$ $16.4\pm$ 10 $9.21\pm$ $0.40$ $16.3\pm$ 10 $9.34\pm$ $0.26$ $16.3\pm$ 10 $9.38\pm$ $0.28$ $16.1\pm$ 10 $8.89\pm$ $0.34*$ $15.6\pm$ | Animals $1 0^6 / \mu \ell$ $g / d\ell$ 10 $9.32 \pm$ $0.36$ $16.4 \pm$ $0.3$ 10 $9.21 \pm$ $0.40$ $16.3 \pm$ $0.3$ 10 $9.34 \pm$ $0.26$ $16.3 \pm$ $0.2$ 10 $9.38 \pm$ $0.28$ $16.1 \pm$ $0.2$ 10 $8.89 \pm$ $0.34 *$ $15.6 \pm$ $0.3 * *$ | Animals $1 0^{6} / \mu l$ $g / dl$ %         10 $9.32 \pm 0.36$ $16.4 \pm 0.3$ $46.8 \pm$ 10 $9.21 \pm 0.40$ $16.3 \pm 0.3$ $46.1 \pm$ 10 $9.34 \pm 0.26$ $16.3 \pm 0.2$ $47.0 \pm$ 10 $9.38 \pm 0.28$ $16.1 \pm 0.2$ $47.1 \pm$ 10 $8.89 \pm 0.34 *$ $15.6 \pm 0.3 * *$ $44.8 \pm$ | Animals $1 0^6 / \mu \ell$ $g / d\ell$ %10 $9.32 \pm 0.36$ $16.4 \pm 0.3$ $46.8 \pm 2.0$ 10 $9.21 \pm 0.40$ $16.3 \pm 0.3$ $46.1 \pm 2.0$ 10 $9.34 \pm 0.26$ $16.3 \pm 0.2$ $47.0 \pm 1.6$ 10 $9.38 \pm 0.28$ $16.1 \pm 0.2$ $47.1 \pm 1.6$ 10 $8.89 \pm 0.34 *$ $15.6 \pm 0.3 * *$ $44.8 \pm 1.7$ | Animals $1 \ 0^6 / \mu \ell$ $g / 4\ell$ % $f \ \ell$ 10 $9.32 \pm \ 0.36$ $16.4 \pm \ 0.3$ $46.8 \pm \ 2.0$ $50.2 \pm$ 10 $9.21 \pm \ 0.40$ $16.3 \pm \ 0.3$ $46.1 \pm \ 2.0$ $50.0 \pm$ 10 $9.34 \pm \ 0.26$ $16.3 \pm \ 0.2$ $47.0 \pm \ 1.6$ $50.3 \pm$ 10 $9.38 \pm \ 0.28$ $16.1 \pm \ 0.2$ $47.1 \pm \ 1.6$ $50.2 \pm$ 10 $8.89 \pm \ 0.34 *$ $15.6 \pm \ 0.3 * *$ $44.8 \pm \ 1.7$ $50.4 \pm$ | Animals $1 0^6 / \mu l$ $g / dl$ % $f l$ 10 $9.32 \pm 0.36$ $16.4 \pm 0.3$ $46.8 \pm 2.0$ $50.2 \pm 0.5$ 10 $9.21 \pm 0.40$ $16.3 \pm 0.3$ $46.1 \pm 2.0$ $50.0 \pm 0.7$ 10 $9.34 \pm 0.26$ $16.3 \pm 0.2$ $47.0 \pm 1.6$ $50.3 \pm 0.7$ 10 $9.38 \pm 0.28$ $16.1 \pm 0.2$ $47.1 \pm 1.6$ $50.2 \pm 0.8$ 10 $8.89 \pm 0.34*$ $15.6 \pm 0.3**$ $44.8 \pm 1.7$ $50.4 \pm 0.9$ | Animals $1 \ 0^6 / \mu^2$ $g / d^2$ % $f \ 2$ $p \ g$ 10 $9.32 \pm \ 0.36$ $16.4 \pm \ 0.3$ $46.8 \pm \ 2.0$ $50.2 \pm \ 0.5$ $17.6 \pm$ 10 $9.21 \pm \ 0.40$ $16.3 \pm \ 0.3$ $46.1 \pm \ 2.0$ $50.0 \pm \ 0.7$ $17.8 \pm$ 10 $9.34 \pm \ 0.26$ $16.3 \pm \ 0.2$ $47.0 \pm \ 1.6$ $50.3 \pm \ 0.7$ $17.5 \pm$ 10 $9.38 \pm \ 0.28$ $16.1 \pm \ 0.2$ $47.1 \pm \ 1.6$ $50.2 \pm \ 0.8$ $17.2 \pm$ 10 $8.89 \pm \ 0.34 *$ $15.6 \pm \ 0.3 * *$ $44.8 \pm \ 1.7$ $50.4 \pm \ 0.9$ $17.6 \pm$ | Animals $10^{6}/\mu^{2}$ $g/4^{2}$ % $f \ell$ $p g$ 10 $9.32 \pm 0.36$ $16.4 \pm 0.3$ $46.8 \pm 2.0$ $50.2 \pm 0.5$ $17.6 \pm 0.7$ 10 $9.21 \pm 0.40$ $16.3 \pm 0.3$ $46.1 \pm 2.0$ $50.0 \pm 0.7$ $17.8 \pm 0.9$ 10 $9.34 \pm 0.26$ $16.3 \pm 0.2$ $47.0 \pm 1.6$ $50.3 \pm 0.7$ $17.5 \pm 0.5$ 10 $9.38 \pm 0.28$ $16.1 \pm 0.2$ $47.1 \pm 1.6$ $50.2 \pm 0.8$ $17.2 \pm 0.5$ 10 $8.89 \pm 0.34*$ $15.6 \pm 0.3**$ $44.8 \pm 1.7$ $50.4 \pm 0.9$ $17.6 \pm 0.8$ | Animals $10^{6}/\mu^{2}$ $g/d^{2}$ % $f^{2}$ $p_{g}$ $g/d^{2}$ 10 $9.32\pm$ $0.36$ $16.4\pm$ $0.3$ $46.8\pm$ $2.0$ $50.2\pm$ $0.5$ $17.6\pm$ $0.7$ $35.2\pm$ 10 $9.21\pm$ $0.40$ $16.3\pm$ $0.3$ $46.1\pm$ $2.0$ $50.0\pm$ $0.7$ $17.8\pm$ $0.9$ $35.6\pm$ 10 $9.34\pm$ $0.26$ $16.3\pm$ $0.2$ $47.0\pm$ $1.6$ $50.3\pm$ $0.7$ $17.5\pm$ $0.5$ $34.7\pm$ 10 $9.38\pm$ $0.28$ $16.1\pm$ $0.2$ $47.1\pm$ $1.6$ $50.2\pm$ $0.8$ $17.2\pm$ $0.5$ $34.3\pm$ 10 $8.89\pm$ $0.34*$ $15.6\pm$ $0.3**$ $44.8\pm$ $1.7$ $50.4\pm$ $0.9$ $17.6\pm$ $0.8$ $34.9\pm$ | Animals $1.0^6 / \mu^2$ $g / d^2$ % $f \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \$ | Animals $1.0^{6}/\mu^{2}$ $g/d^{2}$ $\%$ $f \ 2$ $p \ g$ $g/d^{2}$ $1.0^{3}/\mu^{3}$ $10$ $9.32\pm$ $0.36$ $16.4\pm$ $0.3$ $46.8\pm$ $2.0$ $50.2\pm$ $0.5$ $17.6\pm$ $0.7$ $35.2\pm$ $1.7$ $711\pm$ $10$ $9.21\pm$ $0.40$ $16.3\pm$ $0.3$ $46.1\pm$ $2.0$ $50.0\pm$ $0.7$ $17.8\pm$ $0.9$ $35.6\pm$ $1.6$ $697\pm$ $10$ $9.34\pm$ $0.26$ $16.3\pm$ $0.2$ $47.0\pm$ $1.6$ $50.3\pm$ $0.7$ $17.5\pm$ $0.5$ $34.7\pm$ $1.2$ $708\pm$ $10$ $9.38\pm$ $0.28$ $16.1\pm$ $0.2$ $47.1\pm$ $1.6$ $50.2\pm$ $0.8$ $17.2\pm$ $0.5$ $34.3\pm$ $0.9$ $710\pm$ $10$ $9.38\pm$ $0.34*$ $15.6\pm$ $0.3**$ $44.8\pm$ $1.7$ $50.4\pm$ $0.9$ $17.6\pm$ $0.8$ $34.9\pm$ $1.3$ $769\pm$ |

| roup Name | NO. of<br>Animals | RETICULO<br>‰ | CYTE | PROTHRO<br>sec | MBIN TIME | APTT<br>sec |     |  |
|-----------|-------------------|---------------|------|----------------|-----------|-------------|-----|--|
| 000m      | 10                | 27±           | 5    | 14.8±          | 3.1       | 23.9±       | 2.4 |  |
| 10ppm     | 10                | 23±           | 5    | 14.9±          | 2,2       | 24.9±       | 1   |  |
| 20ppm     | 10                | 23±           | 3    | 14.4±          | 2.6       | 23.5±       | 3.0 |  |
| 40ppm     | 10                | 28±           | 9    | 15.1±          | 3.1       | $24.5\pm$   | .5  |  |
| 80ppm     | 10                | 27±           | 6    | 12.9±          | 1.2       | $23.2\pm$   | .8  |  |
| 160ppm    | 5                 | $30\pm$       | 3    | $13.2\pm$      | 2.6       | 22.8±       | 5.5 |  |

STUDY NO. : 0316 ANIMAL : RAT F344/DuCrj MEASURE. TIME : 1 SEX : MALE

# HEMATOLOGY (SUMMARY) ALL ANIMALS ( 14W)

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### REPORT TYPE : A1

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

| iroup Name  | NO. of<br>Animals | ₩BC<br>1 0³/µ |       | Dif<br>N-BAND | ferentia | L WBC (9<br>N-SEG | 6)   | EOSINO |         | BASO |   | MONO   | · · · · · · · · · · · · · · · · · · · | LYMPHO |     | OTHERS |    |
|-------------|-------------------|---------------|-------|---------------|----------|-------------------|------|--------|---------|------|---|--------|---------------------------------------|--------|-----|--------|----|
| 0pm         | 10                | 6.35±         | 0.91  | 0±            | 0        | $25\pm$           | 4    | 1±     | 1       | 0±   | 0 | 3±     | 1                                     | 71±    | 4   | 0±     | 0  |
| 10ppm       | 10                | 6.49±         | 1.20  | 0±            | 0        | 24±               | 5    | 2±     | 1       | 0±   | 0 | $3\pm$ | 1                                     | 71±    | 7   | 0±     | C  |
| 20pm        | 10                | 6.84±         | 1.21  | 0±            | 0        | $25\pm$           | 6    | 1±     | 1       | 0±   | 0 | 3±     | 1                                     | 71±    | 7   | 0±     | (  |
| 40ppm       | 10                | 6.15±         | 1.07  | 0±            | 0        | 27±               | 6    | 1±     | 1       | 0±   | 0 | 3±     | 1                                     | 69±    | 6   | 0±     | (  |
| 80pm        | 10                | 7.37±         | 2.04  | 0±            | 0        | 30±               | 8    | 1±     | 1       | 0±   | 0 | 4±     | 2                                     | 65±    | 7   | 0±     | (  |
| 160ppm      | 5                 | 4.10±         | 1.99* | 0±            | 0        | 39±               | 10** | 1±     | 1       | 0±   | 0 | 4±     | 2                                     | 56±    | 9** | 0±     | 0  |
| Significant | difference ;      | *:P≦          | 0.05  | **:P≦         | 0.01     |                   |      | Test   | of Dunn | ett  |   |        |                                       |        |     |        |    |
| HCL070)     |                   |               |       |               |          |                   |      |        |         | ·    |   |        |                                       |        |     |        | BA |

APPENDIX E 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

STUDY NO. : 0316 ANIMAL : RAT F344/DuCrj MEASURE. TIME : 1 SEX : MALE REPORT TYPE : A1

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

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| Group Name | NO. of<br>Animals | TOTAL I<br>g∕d¢ | PROTEIN | ALBUMIN<br>g⁄dź |       | A/G RAT       | 10  | T−BILI<br>mg∕dl |      | GLUCOSE<br>mg∕dl |     | T-CHOLES<br>mg∕dl | TEROL | TRIGLYCH<br>mg∕dl | ERIDE |
|------------|-------------------|-----------------|---------|-----------------|-------|---------------|-----|-----------------|------|------------------|-----|-------------------|-------|-------------------|-------|
| 0ppm       | 10                | 6.3±            | 0.1     | 3.9±            | 0.1   | 1.7±          | 0.1 | 0.13±           | 0.01 | $183\pm$         | 11  | $57\pm$           | 7     | 62±               | 13    |
| 10ppm      | 10                | 6.3±            | 0.1     | 4.0±            | 0.1   | 1.7±          | 0.1 | 0.14±           | 0.01 | $182\pm$         | 17  | 62±               | 6     | $52\pm$           | 11    |
| 20ppm      | 10                | 6.3±            | 0.1     | 4.0±            | 0.1   | 1.8±          | 0.1 | 0.13±           | 0.01 | 178±             | 8   | 59±               | 7     | 51±               | 19    |
| 40ppm      | 10                | 6.3±            | 0.1     | 4.0±            | 0.1   | 1.8±          | 0.1 | 0.13±           | 0.01 | 181±             | 7   | 64±               | 6     | 56±               | 15    |
| 80pm       | 10                | 6.4±            | 0.2     | 4.1±            | 0.1*  | 1 <b>.7</b> ± | 0.1 | 0.14±           | 0.01 | 175±             | 9   | $67\pm$           | 9*    | 53±               | 9     |
| 160ppm     | 5                 | 6.3±            | 0.1     | 4.1±            | 0.1** | 1.9±          | 0.1 | 0.14±           | 0.01 | $141\pm$         | 6** | 70±               | 6**   | 24±               | 7**   |
|            |                   |                 |         |                 |       |               |     |                 |      |                  |     |                   |       |                   |       |

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

Test of Dunnett

(HCL074)

BAIS 3

PAGE: 1

STUDY NO. : 0316 ANIMAL : RAT F344/DuCrj MEASURE. TIME : 1 SEX : MALE REPORT TYPE : A1 BIOCHEMISTRY (SUMMARY) ALL ANIMALS ( 14W)

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| oup Name | NO. of<br>Animals | PHOSPHO<br>mg/dl | LIPID | GOT<br>IU/G |    | GPT<br>IU/D | ļ. | LDH<br>IU/G | ]    | ALP<br>IU/Q |    | G-GTP<br>IU∕ℓ |   | CPK<br>IU/Q |    |
|----------|-------------------|------------------|-------|-------------|----|-------------|----|-------------|------|-------------|----|---------------|---|-------------|----|
| 0ppm     | 10                | 107±             | 8     | 68±         | 5  | 43±         | 3  | $155\pm$    | 27   | 297±        | 24 | 2±            | 1 | 111±        | 6  |
| 10ppm    | 10                | 112±             | 6     | 78±         | 20 | 45±         | 8  | 184±        | 62   | $276\pm$    | 16 | 3±            | 1 | 109±        | 10 |
| 20ppm    | 10                | 109±             | 10    | 73±         | 14 | 42±         | 7  | 170±        | 35   | $287\pm$    | 18 | $2\pm$        | 1 | 106±        | 12 |
| 40ppm    | 10                | 114±             | 7     | 78±         | 20 | 44±         | 10 | 187±        | 56   | 284±        | 14 | 2±            | 1 | $113\pm$    | 18 |
| 80ppm    | 10                | 119±             | 11*   | 66±         | 11 | 38±         | 4  | 172±        | 33   | 283±        | 26 | $3\pm$        | 1 | 100±        | 6  |
| 160ppm   | 5                 | $123\pm$         | 13*   | 68±         | 9  | 36±         | 3  | 249±        | 49** | $322 \pm$   | 35 | 2±            | 1 | 115±        | 13 |

(HCL074)

BAIS 3

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STUDY NO. : 0316 ANIMAL : RAT F344/DuCrj MEASURE. TIME : 1 SEX : MALE REPORT TYPE : A1 BIOCHEMISTRY (SUMMARY) ALL ANIMALS ( 14W)

|               | NO. of<br>Animals | UREA NITROGEN<br>mg∕dl |        | CREATININE<br>mg/dl |     | SODIUM<br>mEq∕2 |   | POTASSIUM<br>mEq / D |      | CHLORIDE<br>mEq / D |   | CALCIUM<br>mg⁄dl |       | INORGANIC PHOSPHORU<br>mg/dl |     |
|---------------|-------------------|------------------------|--------|---------------------|-----|-----------------|---|----------------------|------|---------------------|---|------------------|-------|------------------------------|-----|
| 0ppm          | 10                | 19.0±                  | 1.3    | 0.5±                | 0.0 | 141±            | 1 | 3.5±                 | 0.2  | 103±                | 1 | 10.3±            | 0.2   | 5.8±                         | 1.0 |
| 10ppm         | 10                | 19.0±                  | 2.0    | 0.5±                | 0.0 | 141±            | 1 | 3.6±                 | 0.4  | 103±                | 1 | 10.2±            | 0.2   | 5.8±                         | 1.0 |
| 20ppm         | 10                | $18.2\pm$              | 0.9    | 0.5±                | 0.1 | 141±            | 1 | 3.6±                 | 0.2  | 103±                | 1 | 10.3±            | 0.2   | 5.9±                         | 0.9 |
| 40ppm         | 10                | 18.8±                  | 1.2    | 0.5±                | 0.1 | $141\pm$        | 1 | 3.5±                 | 0.2  | 104±                | 2 | 10.2±            | 0.1   | 5.8±                         | 0.8 |
| 80ppm         | 10                | 19.1±                  | 1.4    | 0.5±                | 0.1 | 141±            | 1 | 3.6±                 | 0.2  | 104±                | 1 | 10.3±            | 0.2   | 5.9±                         | 0.7 |
| 160ppm        | 5                 | 19.1±                  | 1.9    | 0.4±                | 0.1 | 140±            | 1 | 3.9±                 | 0.2  | 105±                | 1 | 10.0±            | 0.3** | 6.0±                         | 0.9 |
| Significant d | efference ;       | *:P≦(                  | ).05 * | **:P≦0.0            | 1   |                 |   | Test of Dur          | nett |                     |   |                  |       |                              |     |

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PAGE : 3

### APPENDIX E 2

### BIOCHEMISTRY : SUMMARY, RAT : FEMALE

STUDY NO. : 0316 ANIMAL : RAT F344/DuCrj MEASURE. TIME : 1 SEX : FEMALE REPORT TYPE : A1

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

| up Name | NO. of<br>Animals | TOTAL PROTEIN<br>g/dl |       | ALBUMIN<br>g∕d2 |       | A/G RATIO |       | T-BILIRUBIN<br>mg∕dl |        | GLUCOSE<br>mg⁄dl |     | T-CHOLESTEROL<br>mg∕dl |      | TRIGLYCERIDE<br>mg∕dl |     |
|---------|-------------------|-----------------------|-------|-----------------|-------|-----------|-------|----------------------|--------|------------------|-----|------------------------|------|-----------------------|-----|
| 0ppm    | 10                | 6.2±                  | 0.2   | 3.9±            | 0.1   | 1.7±      | 0.1   | 0.15±                | 0.01   | $137\pm$         | 9   | $71\pm$                | 6    | $14\pm$               | 2   |
| 10ppm   | 10                | 6.0±                  | 0.2*  | 3.8±            | 0.1   | $1.7\pm$  | 0.1   | 0.15±                | 0.01   | $133\pm$         | 15  | 71±                    | 8 .  | $15\pm$               | 2   |
| 20ppm   | 10                | 6.1±                  | 0.1   | 3.9±            | 0.1   | $1.7\pm$  | 0.1   | 0.15±                | 0.01   | $135\pm$         | 9   | 72±                    | 6    | 16±                   | 3   |
| 40ppm   | 10                | 6.0±                  | 0.2*  | 3.9±            | 0.1   | 1.8±      | 0.1   | 0.15±                | 0.01   | 138±             | 12  | $71\pm$                | 11   | $15\pm$               | 3   |
| mqq08   | 10                | 6.0±                  | 0.1*  | 3.8±            | 0.1   | 1.8±      | 0.1   | 0.16±                | 0.01   | $133\pm$         | 11  | 72±                    | 8    | 18±                   | 4   |
| 160ppm  | 2                 | 5.9±                  | 0.1 ? | 3.7±            | 0.3 ? | 1.8±      | 0.4 ? | 0.16±                | 0.01 ? | 116±             | 9 ? | 96±                    | 13 ? | 29±                   | 4 ? |

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

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BAIS 3

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STUDY NO. : 0316 ANIMAL : RAT F344/DuCrj MEASURE. TIME : 1 SEX : FEMALE REPORT TYPE : A1 ~\_\_\_\_

| oup Name<br>Oppm | NO. of<br>Animals | PHOSPHOLIPID<br>mg/dl |     | GOT<br>IU∕₽ |     | GPT<br>IU∕₽ |     | LDH<br>IU/l |      | ALP<br>IU∕Q |     | G-GTP<br>IU∕ℓ |     | CPK<br>IU/2 |     |
|------------------|-------------------|-----------------------|-----|-------------|-----|-------------|-----|-------------|------|-------------|-----|---------------|-----|-------------|-----|
|                  | 10                | 133±                  | 8   | 72±         | 10  | 39±         | 11  | 309±        | 106  | $205\pm$    | 32  | 3±            | 1   | 140±        | 24  |
| 10ppm            | 10                | 129±                  | 12  | 64±         | 3   | 32±         | 4   | 283±        | 61   | 200±        | 24  | 2±            | 1   | $127\pm$    | 17  |
| 20ppm            | 10                | $135\pm$              | 10  | 69±         | 5   | 36±         | 4   | $246\pm$    | 31   | 219±        | 16  | 3±            | 1   | $122\pm$    | 17  |
| 40ppm            | 10                | 130±                  | 13  | 71±         | 6   | 37±         | 5   | $265\pm$    | 40   | 203±        | 23  | 3±            | 1   | $123\pm$    | 9   |
| 80ppm            | 10                | 134±                  | 13  | $65\pm$     | 5   | 32±         | 5   | 293±        | 98   | 217±        | 31  | 3±            | 1   | $128\pm$    | 29  |
| 160ppm           | 2                 | $177\pm$              | 6 ? | 81±         | 2 ? | 39±         | 1 ? | 359±        | 33 ? | $311\pm$    | 3 ? | 6±            | 1 ? | $121\pm$    | 4 ? |

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

(HCL074)

STUDY NO. : 0316 ANIMAL : RAT F344/DuCrj MEASURE. TIME : 1 SEX : FEMALE REPORT TYPE : A1

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

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| oup Name | NO. of<br>Animals | UREA N<br>mg/dl | TROGEN | CREATININE<br>mg∕d£ |       | SODIUM<br>mEq⁄Q |     | POTASSIUM<br>mEq⁄l |       |      | 3   | CALCIU<br>mg⁄dl |       | INORGANIC PHOSPHOR<br>mg/dl |       |  |
|----------|-------------------|-----------------|--------|---------------------|-------|-----------------|-----|--------------------|-------|------|-----|-----------------|-------|-----------------------------|-------|--|
| maq0     | 10                | 19.2±           | 2.3    | 0.6±                | 0.1   | 141±            | 2   | 3.5±               | 0.3   | 106± | 2   | 10.1±           | 0.2   | 5.0±                        | 1.5   |  |
| 10ppm    | 10                | 17.7±           | 1.3    | 0.5±                | 0.0   | 140±            | 2   | 3.5±               | 0.2   | 104± | 2   | 10.0±           | 0.1   | 4.9±                        | 1.4   |  |
| 20ppm    | 10                | 17.9±           | 1.6    | 0.5±                | 0.0   | $140\pm$        | 1   | 3.5±               | 0.2   | 104± | 2   | 10.0±           | 0.2   | 5.0±                        | 1.2   |  |
| 40ppm    | 10                | 17.9±           | 1.2    | 0.5±                | 0.0*  | $141\pm$        | 1   | 3.3±               | 0.3   | 105± | 1   | 9.9±            | 0.1   | 5.1±                        | 0.8   |  |
| 80ppm    | 10                | 17.0±           | 2.3    | 0.5±                | 0.0** | $141\pm$        | 1   | 3.5±               | 0.2   | 106± | 2   | 9.9±            | 0.2   | 5.7±                        | 1.1   |  |
| 160ppm   | 2                 | 15.6±           | 0.4 ?  | 0.4±                | 0.0 ? | $138\pm$        | 1 ? | 4.0±               | 0.3 ? | 102± | 3 ? | 9.7±            | 0.2 ? | 5.5±                        | 0.8 ? |  |

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

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APPENDIX F 1

URINALYSIS : SUMMARY, RAT: MALE

| o Name | NO. of<br>Animals | pH | 6.0 | 6.5 | 7 0 | 7.5 | 8.0 | 8.5 CHI | Prot |          |   | + 3+ | 4+ | CHI |    | ucos |   | 4 94 | - 4+ | CHI |   |   | bady<br>+ 2+ |   | 1+ | CHI |    | liruk | oin<br>2+3+ | CHI |
|--------|-------------------|----|-----|-----|-----|-----|-----|---------|------|----------|---|------|----|-----|----|------|---|------|------|-----|---|---|--------------|---|----|-----|----|-------|-------------|-----|
|        |                   |    |     |     |     |     |     |         |      | <u>+</u> |   |      |    |     |    |      |   |      |      |     |   |   |              |   |    |     |    |       |             |     |
| 0ppm   | 10                | 0  | 1   | 1   | 3   | 2   | 2   | 1       | 0    | 5        | 3 | 20   | 0  |     | 10 | 0    | 0 | 0 0  | ) () |     | 9 | 1 | 0 0          | 0 | 0  |     | 10 | 0     | 0 0         |     |
| 10ppm  | 10                | 0  | 1   | 0   | 3   | 2   | 4   | 0       | 1    | 5        | 3 | 1 0  | 0  |     | 10 | 0    | 0 | 0 0  | 0    |     | 7 | 2 | 1 0          | 0 | 0  |     | 10 | 0     | 0 0         |     |
| 20ppm  | 10                | 0  | 0   | 0   | 3   | 3   | 3   | 1       | 0    | 1        | 9 | 0 0  | 0  | *   | 10 | 0    | 0 | 0 (  | 0 0  |     | 7 | 3 | 0 0          | 0 | 0  |     | 10 | 0     | 0 0         |     |
| 40ppm  | 10                | 0  | 0   | 0   | 1   | 3   | 5   | 1       | 0    | 7        | 3 | 0 0  | 0  |     | 10 | 0    | 0 | 0 0  | 0 (  |     | 8 | 2 | 0 0          | 0 | 0  |     | 10 | 0     | 0 0         |     |
| 80ppm  | 10                | 0  | 0   | 0   | 0   | 2   | 5   | 3       | 0    | 3        | 5 | 2 0  | 0  |     | 10 | 0    | 0 | 0 0  | 0 (  |     | 4 | 5 | 1 0          | 0 | 0  |     | 10 | 0     | 0 0         |     |
| 160ppm | 5                 | 0  | 0   | 0   | 0   | 0   | 2   | 3       | 0    | 0        | 0 | 50   | 0  | *   | 5  | 0    | 0 | 0 (  | ) () |     | 0 | 2 | 2 1          | 0 | 0  | **  | 5  | 0     | 0 0         |     |

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URINALYSIS

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STUDY NO. : 0316 ANIMAL : RAT F344/DuCrj MEASURE. TIME : 1

| roup Name   | NO. of<br>Animals | 0ccult blood<br>- ± + 2+ 3+ CHI | Urabilinogen<br>± + 2+ 3+ 4+ CHI |                    |  |
|-------------|-------------------|---------------------------------|----------------------------------|--------------------|--|
| 0ppm        | 10                | 10 0 0 0 0                      | 10 0 0 0 0                       |                    |  |
| 10ppm       | 10                | 10 0 0 0 0                      | 10 0 0 0 0                       |                    |  |
| 20ppm       | 10                | 90100                           | 10 0 0 0 0                       |                    |  |
| 40ppm       | 10                | 10 0 0 0 0                      | 10 0 0 0 0                       |                    |  |
| 80ppm       | 10                | 8 1 0 0 1                       | 10 0 0 0 0                       |                    |  |
| 160ppm      | 5                 | 5 0 0 0 0                       | 5 0 0 0 0                        |                    |  |
| Significant | difference        | ; *:P≦0.05 *                    | F : P ≤ 0.01                     | Test of CHI SQUARE |  |

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APPENDIX F 2

URINALYSIS : SUMMARY, RAT : FEMALE

| up Name  | NO. of<br>Animals | рН <u></u><br>5.0 | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 | CHI |   | ote<br>± |   | 2+ ; | 3+ 4+ | СН | I | Glu |   |     | + 3+ | 4+ | CHI |    |   | body<br>+ 2+ |      | 4+ | CHI | Bili<br>— - |     | n<br>• 3+ | CH | I |
|----------|-------------------|-------------------|-----|-----|-----|-----|-----|-----|-----|---|----------|---|------|-------|----|---|-----|---|-----|------|----|-----|----|---|--------------|------|----|-----|-------------|-----|-----------|----|---|
|          |                   |                   |     |     |     |     |     | -   |     |   |          | - |      |       |    |   |     |   |     | -    |    |     |    |   |              |      |    |     | <br>        |     |           |    |   |
| 0<br>ppm | 10                | 0                 | 0   | 1   | 0   | 2   | 6   | 1   |     |   | 44       | 2 | 0    | 0 0   |    |   | 10  | 0 | 0 ( | 0 0  | 0  |     | 10 | 0 | 0 0          | ) 0  | 0  |     | 10          | 0 ( | 0         |    |   |
| 10ppm    | 10                | 0                 | 1   | 0   | 0   | 1   | 6   | 2   |     | ; | 34       | 3 | 0    | 0 0   |    |   | 10  | 0 | 0 ( | 0 0  | 0  |     | 10 | 0 | 0 0          | ) 0  | 0  |     | 10          | 0 ( | 0         |    |   |
| 20ppm    | 10                | 0                 | 0   | 0   | 0   | 5   | 3   | 2   |     | : | 27       | 1 | 0    | 0 0   |    |   | 10  | 0 | 0 ( | 0 0  | 0  |     | 10 | 0 | 0 0          | ) () | 0  |     | 10          | 0 ( | 0         |    |   |
| 40ppm    | 10                | 0                 | 0   | 0   | 6   | 2   | 2   | 0   | *   |   | 17       | 2 | 0    | 0 0   |    |   | 10  | 0 | 0 0 | 0 0  | 0  |     | 10 | 0 | 0 0          | ) 0  | 0  |     | 10          | 0 ( | 0         |    |   |
| 80ppm    | 10                | 0                 | 0   | 0   | 2   | 1   | 4   | 3   |     | : | 36       | 1 | 0    | 0 0   |    |   | 10  | 0 | 0 ( | 0 0  | 0  |     | 10 | 0 | 0 0          | ) 0  | 0  |     | 10          | 0 ( | ) ()      |    |   |
| 160ppm   | 2                 | 0                 | 1   | 1   | 0   | 0   | 0   | 0   | ?   | 1 | 0 0      | 2 | 0    | 0 0   |    | ? | 2   | 0 | 0 ( | 0 0  | 0  | ?   | 1  | 0 | 0 1          | 0    | 0  | ?   | 2           | 0 ( | 0 0       |    | ? |

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

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BAIS 3

#### URINALYSIS

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STUDY NO. : 0316 ANIMAL : RAT F344/DuCrj MEASURE, TIME : 1 SE

| up Name | NO. of<br>Animals | Occult blood<br>— ± + 2+ 3+ CHI | Urobilinogen<br>± + 2+ 3+ 4+ CHI |  |
|---------|-------------------|---------------------------------|----------------------------------|--|
| 0ppm    | 10                | 10 0 0 0 0                      | 10 0 0 0 0                       |  |
| 10ppm   | 10                | 10 0 0 0 0                      | 10 0 0 0 0                       |  |
| 20ppm   | 10                | 10 0 0 0 0                      | 10 0 0 0 0                       |  |
| 40ppm   | 10                | 10 0 0 0 0                      | 10 0 0 0 0                       |  |
| 80ppm   | 10                | 10 0 0 0 0                      | 10 0 0 0 0                       |  |
| 160ppm  | 2                 | 20000?                          | 20000?                           |  |

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BAIS 3

# APPENDIX A 1

# CLINICAL OBSERVATION : SUMMARY, RAT : MALE

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, RAT : MALE

# APPENDIX B 2

# BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

# APPENDIX C 1

# FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

# APPENDIX C 2

# FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

APPENDIX D 1

HEMATOLOGY : SUMMARY, RAT : MALE

APPENDIX D 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

APPENDIX E 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

# APPENDIX E 2

# BIOCHEMISTRY : SUMMARY, RAT : FEMALE

# APPENDIX F 1

# URINALYSIS : SUMMARY, RAT : MALE

APPENDIX F 2

URINALYSIS : SUMMARY, RAT : FEMALE

GROSS FINDINGS : SUMMARY, RAT : MALE

DEAD AND MORIBUND ANIMALS

# GROSS FINDINGS : SUMMARY, RAT : MALE : SACRIFICED ANIMALS (13 - WEEK STUDY)

GROSS FINDINGS : SUMMARY, RAT : FEMALE

DEAD AND MORIBUND ANIMALS

# GROSS FINDINGS : SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS (13 - WEEK STUDY)

APPENDIX H 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

# APPENDIX H 2

# ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

APPENDIX I 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

APPENDIX I 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

APPENDIX J 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : DEAD AND MORIBUND ANIMALS

#### APPENDIX J 2

#### HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE: SACRIFICED ANIMALS

(13 - WEEK STUDY)

**RAT : FEMALE : DEAD AND MORIBUND ANIMALS** 

# APPENDIX J 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

#### APPENDIX J 4

#### HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : SACRIFICED ANIMALS

APPENDIX K 1

IDENTITY OF GLYCIDOL IN THE 13 - WEEK INHALATION STUDY

APPENDIX K 2

STABILITY OF GLYCIDOL IN THE 13 - WEEK INHALATION STUDY

APPENDIX L 1

# CONCENTRATION OF GLYCIDL IN THE INHALATION CHAMBER OF THE 13-WEEK INHALATION STUDY

#### APPENDIX L 2

# ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13 - WEEK INHALATION STUDY OF GLYCIDOL

# APPENDIX M 1

# METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE 13 - WEEK INHALATION STUDY OF GLYCIDOL

## APPENDIX M 2

# UNITS AND DECIMARL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13 - WEEK INHALATION STUDY OF GLYCIDOL

| STUDY NO. : 0316<br>ANIMAL : RAT F344/DuCrj<br>REPORT TYPE : A1<br>SEX : MALE | GROSS FINDINGS (SUMMARY)<br>DEAD AND MORIBUND ANIMALS (O- 14W) |                        |                |                |  |  |  |  |
|-------------------------------------------------------------------------------|----------------------------------------------------------------|------------------------|----------------|----------------|--|--|--|--|
| Organ Findings                                                                | Group Name<br>NO. of Animals 0 (%                              | 0ppm 10ppm<br>5) 0 (%) | 20ppm<br>0 (%) | 40ppm<br>0 (%) |  |  |  |  |
| thymus atrophic                                                               | - (                                                            | -) - ( -)              | - ( -)         | - ( -)         |  |  |  |  |
| (HPT080)                                                                      |                                                                |                        |                | BAIS 3         |  |  |  |  |

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| STUDY NO. : 0316<br>ANIMAL : RAT F344/DuCrj<br>REPORT TYPE : A1<br>SEX : MALE | GROSS FINDINGS (SUMMARY)<br>DEAD AND MORIBUND ANIMALS (0- 14W) | PAGE : 2 |
|-------------------------------------------------------------------------------|----------------------------------------------------------------|----------|
| Organ Findings                                                                | Group Name 80ppm 160ppm<br>NO. of Animals 0 (%) 5 (%)          |          |
| thymus atrophic                                                               | - ( -) 1 ( 20)                                                 |          |
| (HPT080)                                                                      |                                                                | BAIS 3   |

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## APPENDIX G 2

# GROSS FINDINGS : SUMMARY, RAT : MALE : SACRIFICED ANIMALS (13 - WEEK STUDY)

| STUDY NO. : 0316        | GROSS FINDINGS (SUMMARY)  |
|-------------------------|---------------------------|
| ANIMAL : RAT F344/DuCrj | SACRIFICED ANIMALS ( 14W) |
| REPORT TYPE : A1        |                           |
| SEX : MALE              |                           |

# Y) 4W)

### PAGE: 1

| 0rgan      | Findings   | Group Name<br>NO. of Animals | 0ppm<br>10 (%) | 10ppm<br>10 (%) | 20ppm<br>10 (%) | 40ppm<br>10 (%) |
|------------|------------|------------------------------|----------------|-----------------|-----------------|-----------------|
| lymph node | enlarged   |                              | 0 ( 0)         | 0 ( 0)          | 0 ( 0)          | 0 ( 0)          |
| Liver      | hermiation |                              | 0 ( 0)         | 1 ( 10)         | 0 ( 0)          | 0 ( 0)          |

(HPT080)

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BAIS 3

| STUDY NO. : 0316        | GROSS FINDINGS (SUMMARY)  |
|-------------------------|---------------------------|
| ANIMAL : RAT F344/DuCrj | SACRIFICED ANIMALS ( 14W) |
| REPORT TYPE : A1        |                           |
| SEX : MALE              |                           |

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| Organ               | Findings               | Group Name<br>NO. of Animals | 80ppm<br>10 (%) | 160ppm<br>5 (%)  |  |
|---------------------|------------------------|------------------------------|-----------------|------------------|--|
| lymph node<br>liver | enlarged<br>herniation |                              | 1 (10)<br>0 (0) | 0 ( 0)<br>0 ( 0) |  |

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(HPT080)

BAIS 3

APPENDIX G 3

GROSS FINDINGS : SUMMARY, RAT : FEMALE

DEAD AND MORIBUND ANIMALS

(13 - WEEK STUDY)

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

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STUDY NO. : 0316 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

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#### PAGE : 3

| Organ    | Findings               | Group Name<br>NO. of Animals | 0ppm<br>0 (%) | 10 ממסס<br>(%) 0 | 20ppm<br>0 (%) | 40ppm<br>0 (%) |
|----------|------------------------|------------------------------|---------------|------------------|----------------|----------------|
| hymus    | atrophic               |                              | - ( -)        | - ( -)           | - ( -)         | - ( -)         |
| in bladd | urine:marked retention |                              | - ( -)        | - ( -)           | - ( -)         | - ( -)         |

| ANIMAL :<br>REPORT TYPE : | : 0316<br>: RAT F344/DuCrj<br>: A1<br>: FEMALE |                              |                |                 |  |  |  |
|---------------------------|------------------------------------------------|------------------------------|----------------|-----------------|--|--|--|
| Organ                     | Findings                                       | Group Name<br>NO. of Animals | 80ppm<br>0 (%) | 160ppm<br>8 (%) |  |  |  |
| thymus                    | atrophic                                       |                              | - ( -)         | 3 (38)          |  |  |  |
| urin bladd                | urine:marked retention                         |                              | - ( -)         | 1 (13)          |  |  |  |
|                           |                                                |                              |                |                 |  |  |  |

(HPT080)

BAIS 3

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# APPENDIX G 4

# GROSS FINDINGS : SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS (13 - WEEK STUDY)

| STUDY NO. :   | : 0316         | GROSS FINDINGS (SUMMARY) |
|---------------|----------------|--------------------------|
| ANIMAL :      | RAT F344/DuC-j | SACRIFICED ANIMALS ( 14W |
| REPORT TYPE : | : A1           |                          |
| SEX :         | ; FEMALE       |                          |

| Organ  | Findings   | Group Name<br>NO. of Animals | 0ppm<br>0 (%)<br>0 | 10ppm<br>10 (%) | 20ppm<br>10 (%) | 40ppm<br>10 (%) |
|--------|------------|------------------------------|--------------------|-----------------|-----------------|-----------------|
| liver  | herniation |                              | 0 ( 0)             | 1 (10)          | 1 (10)          | 0 ( 0)          |
| uterus | nodule     |                              | 0 ( 0)             | 0 ( 0)          | 1 (10)          | 0 ( 0)          |
| өуө    | white      |                              | 0 ( 0)             | 0 ( 0)          | 1 (10)          | 0 ( 0)          |

(HPT080)

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# Y) 4W)

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#### GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS ( 14W)

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STUDY NO. : 0316 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

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| 0rgan  | Findings   | Group Name 80ppm<br>NO. of Animals 10 (%) | 160ppm<br>2 (%) |
|--------|------------|-------------------------------------------|-----------------|
| liver  | herniation | 3 (30)                                    | 0 ( 0)          |
| uterus | nodule     | 0 ( 0)                                    | 0 ( 0)          |
| өуө    | white      | 0 ( 0)                                    | 0 ( 0)          |
|        |            |                                           |                 |

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APPENDIX H 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

5

160ppm

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

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0.085± 0.027\*\*

| UNIT: g    |                   |          |        |        |         |        |       |             |       |        |       |        |       | PAGE : 1 |
|------------|-------------------|----------|--------|--------|---------|--------|-------|-------------|-------|--------|-------|--------|-------|----------|
| Group Name | NO. of<br>Animals | Body (   | Weight | THYM   | IS      | ADRE   | NALS  | TEST        | ES    | HEAR'  | Г     | LUNG   | S     |          |
| 000m       | 10                | 273±     | 18     | 0.219± | 0.029   | 0.050± | 0.006 | 2.908±      | 0.113 | 0.900± | 0.073 | 0.940± | 0.069 |          |
| 1000m      | 10                | 260±     | 9      | 0.212± | 0.022   | 0.050± | 0.007 | $2.806 \pm$ | 0.099 | 0.853± | 0.033 | 0.895± | 0.038 |          |
| 2000m      | 10                | $254\pm$ | 15*    | 0.205± | 0.030   | 0.051± | 0.006 | $2.844 \pm$ | 0.092 | 0.897± | 0.069 | 0.916± | 0.039 |          |
| 400m       | 10                | $251\pm$ |        | 0.193± | 0.026   | 0.051± | 0.004 | $2.850 \pm$ | 0.150 | 0.863± | 0.064 | 0.915± | 0.047 |          |
| 80ppm      | 10                | 233±     | 11**   | 0.175± | 0.024** | 0.052± | 0.004 | $2.654\pm$  | 0.496 | 0.870± | 0.028 | 0.937± | 0.056 |          |

0.040土 0.002\*\*

0.890± 0.058\*\*

Test of Dunnett

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0.593± 0.047\*\* 0.719± 0.072\*\*

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

128± 15\*\*

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BAIS 3

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

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| oup Name | NO. of<br>Animals | KID         | NEYS    | SPL    | EEN     | LIV        | ER      | BRA        | N       |  |
|----------|-------------------|-------------|---------|--------|---------|------------|---------|------------|---------|--|
|          |                   |             |         |        |         |            |         | . <u></u>  |         |  |
| 0ppm     | 10                | $1.683 \pm$ | 0.086   | 0.495± | 0.046   | 6.773±     | 0.446   | 1.847±     | 0.040 . |  |
| 10ppm    | 10                | 1.657±      | 0.056   | 0.479± | 0.023   | $6.512\pm$ | 0.348   | $1.853\pm$ | 0.046   |  |
| 20ppm    | 10                | 1.682±      | 0.096   | 0.484± | 0.041   | 6.443±     | 0.488   | 1.826±     | 0.051   |  |
| 40ppm    | 10                | 1.684±      | 0.092   | 0.493± | 0.040   | 6.561±     | 0.313   | $1.820\pm$ | 0.054   |  |
| 80ppm    | 10                | 1.777±      | 0.115   | 0.496± | 0.026   | 6.432±     | 0.449   | $1.794\pm$ | 0.039   |  |
| 160ppm   | 5                 | 1.409±      | 0.087** | 0.281± | 0.058** | 4.047±     | 0.478** | $1.566\pm$ | 0.064** |  |

Test of Dunnett

(HCL040)

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

BAIS 3

# APPENDIX H 2

# ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

0ppm

10ppm

20ppm

40ppm

80ppm

Group Name

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

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NO. of Body Weight THYMUS ADRENALS OVARIES HEART LUNGS Animals 10  $163 \pm$ 8 0.181± 0.013 0.058± 0.011 0.106± 0.018 0.602± 0.032 0.731± 0.046 10  $153\pm$ 9\* 0.172± 0.012  $0.054 \pm 0.006$ 0.095± 0.010 0.595± 0.036 0.716± 0.052 10  $148\pm$ 8\*\* 0.164± 0.021 0.051± 0.008  $0.097 \pm 0.014$ 0.605± 0.062 0.676± 0.029\*\* 10  $142\pm$ 8\*\* 0.154± 0.021\*\* 0.054± 0.007  $0.094 \pm 0.015$ 0.569± 0.039 0.697± 0.032 10  $140\pm$ 7\*\* 0.148± 0.034\*\* 0.049± 0.008 0.099± 0.019 0.699± 0.030 0.572± 0.031

160ppm 2 91± 1 ? 0.080± 0.012 ? 0.043± 0.001 ? 0.045± 0.001 ? 0.502± 0.049 ? 0.583± 0.046 ?

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

Test of Dunnett

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

(HCL040)

BAIS 3

#### PAGE : 3

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

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| Group Name  | NO. of<br>Animals | KID     | NEYS    | SPL        | EEN      | LIV        | ER      | BRA         | IN      | <br> |
|-------------|-------------------|---------|---------|------------|----------|------------|---------|-------------|---------|------|
| 0ppm        | 10                | 1.057±  | 0.047   | 0.359±     | 0.015    | 3.849±     | 0.265   | 1.698±      | 0.135   |      |
| 10ppm       | 10                | 1.085±  | 0.068   | 0.353±     | 0.021    | $3.631\pm$ | 0,246   | 1.734±      | 0.038   |      |
| 20ppm       | 10                | 1.086±  | 0.042   | 0.342±     | 0.030    | $3,605\pm$ | 0.217   | 1.699±      | 0.033   |      |
| 40ppm       | 10                | 1.119±  | 0.043   | 0.335±     | 0.023    | 3.467±     | 0.148** | $1.692 \pm$ | 0.017*  |      |
| 80pm        | 10                | 1.207±  | 0.077** | $0.347\pm$ | 0.026    | 3.649±     | 0.286   | $1.687\pm$  | 0.030** |      |
| 160ppm      | 2                 | 1.246±  | 0.047 ? | 0.222±     | 0.010 ?  | $2.855\pm$ | 0.054 ? | $1.469\pm$  | 0.030 ? |      |
| Significant | difference ;      | *:P≦0.0 | 05 ** : | P ≦ 0.01   | <u>.</u> |            | Tes     | t of Dunnet | t       |      |

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

(HCL040)

BAIS 3

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APPENDIX I 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

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

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PAGE : 1

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| -oup Name   | NO. of<br>Animals | Body We<br>(g |      | THYMUS       | ADRENALS       | TESTES            | HEART          | LUNGS          |  |
|-------------|-------------------|---------------|------|--------------|----------------|-------------------|----------------|----------------|--|
| 0ppm        | 10                | 273± 1        | 18   | 0.081± 0.009 | 0.018± 0.003   | 1.070± 0.066      | 0.330± 0.012   | 0.345± 0.015   |  |
| 10ppm       | 10                | 260±          | 9    | 0.082± 0.009 | 0.019± 0.003   | 1.079± 0.030      | 0.328± 0.010   | 0.345± 0.015   |  |
| 20ppm       | 10                | 254±          | 15*  | 0.081± 0.011 | 0.020± 0.003   | 1.125± 0.074      | 0.354± 0.022   | 0.362± 0.015   |  |
| 40ppm       | 10                | <b>25</b> 1±  | 14** | 0.077± 0.008 | 0.020± 0.002   | 1.137± 0.056      | 0.344± 0.016   | 0.365± 0.011   |  |
| 80ppm       | 10                | 233± 3        | 11** | 0.075± 0.009 | 0.023± 0.002** | 1.140± 0.217*     | 0.374± 0.013** | 0.402± 0.021** |  |
| 160ppm      | 5                 | 128±          | 15** | 0.066± 0.014 | 0.032± 0.003** | $0.704 \pm 0.088$ | 0.467± 0.043** | 0.565± 0.029** |  |
| Significant | difference ;      | *:P≦0.05      | **   | : P ≦ 0.01   | Test           | of Dunnett        |                |                |  |
| CL042)      |                   |               |      |              |                |                   |                | <u> </u>       |  |

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

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PAGE: 2

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| -oup Name   | NO. of<br>Animals | KIDNEYS        | SPLEEN         | LIVER          | BRAIN          |  |
|-------------|-------------------|----------------|----------------|----------------|----------------|--|
| 0ppm        | 10                | 0.618± 0.023   | 0.181± 0.007   | 2.486± 0.046   | 0.680± 0.037   |  |
| 10pm        | 10                | 0.637± 0.015   | 0.184± 0.004   | 2.503± 0.079   | 0.713± 0.019   |  |
| 20ppm       | 10                | 0.664± 0.022*  | 0.191± 0.009   | 2.538± 0.072   | 0.721± 0.036   |  |
| 40ppm       | 10                | 0.672± 0.015** | 0.197± 0.013*  | 2.616± 0.054** | 0.727± 0.034   |  |
| 80ppm       | 10                | 0.762± 0.027** | 0.213± 0.007** | 2.758± 0.114** | 0.771± 0.032** |  |
| 160ppm      | 5                 | 1.111± 0.089** | 0.218± 0.022** | 3.173± 0.099** | 1.235± 0.090** |  |
| Significant | difference ;      | *:P≦0.05 **:   | P ≦ 0.01       | Test           | of Dunnett     |  |
| ICL042)     |                   |                |                | ·····          |                |  |

APPENDIX I 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

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

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PAGE : 3

| Group Name | NO. of<br>Animals | Body W<br>( | eight<br>g) | THYMUS         | ADRENALS       | OVARIES        | HEART          | LUNGS          |
|------------|-------------------|-------------|-------------|----------------|----------------|----------------|----------------|----------------|
| 0ppm       | 10                | 163±        | 8           | 0.111± 0.007   | 0.035± 0.006   | 0.065± 0.010   | 0.369± 0.021   | 0.448± 0.025   |
| 10ppm      | 10                | 153±        | 9*          | 0.113± 0.010   | 0.035± 0.004   | 0.062± 0.007   | 0.390± 0.024   | 0.469± 0.023   |
| 20ppm      | 10                | 148±        | 8**         | 0.110± 0.013   | 0.035± 0.005   | 0.065± 0.009   | 0.408± 0.023** | 0.458± 0.022   |
| 40ppm      | 10                | $142\pm$    | 8**         | 0.109± 0.015   | 0.038± 0.005   | 0.066± 0.010   | 0.402± 0.015** | 0.493± 0.028** |
| 80ppm      | 10                | $140\pm$    | 7**         | 0.106± 0.025   | 0.035± 0.005   | 0.071± 0.015   | 0.410± 0.020** | 0.501± 0.018** |
| 160ppm     | 2                 | 91±         | 1 ?         | 0.088± 0.012 ? | 0.047± 0.001 ? | 0.049± 0.001 ? | 0.551± 0.045 ? | 0.641± 0.060 ? |

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

(HCL042)

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

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PAGE: 4

| Group Name | NO. of<br>Animals | KIDNEYS        | SPLEEN         | LIVER          | BRAIN          |
|------------|-------------------|----------------|----------------|----------------|----------------|
| 0ppm       | 10                | 0.648± 0.031   | 0.220± 0.014   | 2.358± 0.103   | 1.042± 0.094   |
| 10ppm      | 10                | 0.711± 0.029** | 0.231± 0.015   | 2.376± 0.061   | 1.138± 0.066** |
| 20ppm      | 10                | 0.735± 0.028** | 0.231± 0.023   | 2.436± 0.042   | 1.151± 0.062** |
| 40ppm      | 10                | 0.792± 0.034** | 0.237± 0.012   | 2.453± 0.091   | 1.199± 0.058** |
| 80ppm      | 10                | 0.865± 0.027** | 0.249± 0.014** | 2.614± 0.116** | 1.211± 0.044** |
| 160ppm     | 2                 | 1.369± 0.030 ? | 0.244± 0.014 ? | 3.137± 0.011 ? | 1.615± 0.008 ? |

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

(HCL042)

BAIS 3

APPENDIX J 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : DEAD AND MORIBUND ANIMALS

(13 - WEEK STUDY)

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

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

| 0rgan          | No                                       | roup Name 0ppm<br>0. of Animals on Study 0<br>rade <u>1 2 3 4</u><br>(%) (%) (%) (%) | 10ppm<br>0<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} & 20 \text{ppm} \\ 0 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $\begin{array}{c} & 40 \text{ppm} \\ 0 & 0 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ |
|----------------|------------------------------------------|--------------------------------------------------------------------------------------|-------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------|
| [Respiratory : | system]                                  |                                                                                      |                                                 |                                                                                                                 |                                                                                                                     |
| nasal cauit    | adhesion                                 | < 0><br>                                                                             | < 0><br>                                        | < 0><br><br>( -) ( -) ( -) ( -)                                                                                 | < 0><br>                                                                                                            |
|                | inflammatory infiltration                | ( -) ( -) ( -) ( -)                                                                  | ( -) ( -) ( -) ( -)                             | ( -) ( -) ( -) ( -)                                                                                             | ( -) ( -) ( -) ( -)                                                                                                 |
|                | respiratory metaplasia:olfactory epithel | ium                                                                                  | ( -) ( -) ( -) ( -)                             | ( -) ( -) ( -) ( -)                                                                                             | ( -) ( -) ( -) ( -)                                                                                                 |
|                | squamous cell metaplasia:respiratory epi | thelium                                                                              | ( -) ( -) ( -) ( -)                             | ( -) ( -) ( -) ( -)                                                                                             | ( -) ( -) ( -) ( -)                                                                                                 |
|                | atrophy:turbinate                        | ( -) ( -) ( -) ( -)                                                                  | ( -) ( -) ( -) ( -)                             | ( -) ( -) ( -) ( -)                                                                                             | ( -) ( -) ( -) ( -)                                                                                                 |
|                | ulcer:respiratory epithelium             | ( -) ( -) ( -) ( -)                                                                  | ( -) ( -) ( -) ( -)                             | ( -) ( -) ( -) ( -)                                                                                             | ( -) ( -) ( -) ( -)                                                                                                 |
|                | atrophy:olfactory epithelium             | ( -) ( -) ( -) ( -)                                                                  | ( -) ( -) ( -) ( -)                             | ( -) ( -) ( -) ( -)                                                                                             | ( -) ( -) ( -) ( -)                                                                                                 |
|                | erosion:respiratory epithelium           | ( -) ( -) ( -) ( -)                                                                  | ( -) ( -) ( -) ( -)                             | ( -) ( -) ( -) ( -)                                                                                             | ( -) ( -) ( -) ( -)                                                                                                 |

Grade 1: Slight 2: Moderate 3: Marked 4: Severe

< a > a : Number of animals examined at the site

b b: Number of animals with lesion

(c) c:b/a\*100

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

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| 0rgan        |                                        | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | ( <u>2</u><br>(%) | 80pp<br>)<br>3<br>(%) | om<br><u>4</u><br>(%) | <u>1</u><br>(%) | 2 (%)          | 160p<br>5<br>3<br>(%) | pm<br><u>4</u><br>(%) |  |
|--------------|----------------------------------------|----------------------------------------------------------------|-------------------|-----------------------|-----------------------|-----------------|----------------|-----------------------|-----------------------|--|
| [Respiratory | system]                                |                                                                |                   |                       |                       |                 |                |                       |                       |  |
| nasal cavit  | adhesion                               | - ( -)                                                         | < (<br>           | )><br>_<br>( -)       | -<br>( -)             | 1<br>(20)       | <<br>0<br>( 0) | 5><br>0<br>( 0)       | 0<br>( 0)             |  |
|              | inflammatory infiltration              | ( -)                                                           | - ( -)            | -<br>()               | -<br>()               | 3<br>(60)       | 2<br>(40)      | 0<br>( 0)             | 0<br>( 0)             |  |
|              | respiratory metaplasia:olfactory epith | elium –<br>(-)                                                 | -<br>( -)         | -<br>( -)             | -<br>( -)             | 0<br>( 0)       | 1<br>(20)      | 0<br>( 0)             | 0<br>(0)              |  |
|              | squamous cell metaplasia:respiratory e | pithelium -<br>(-)                                             |                   | -<br>( -)             | -<br>( -)             | 0<br>( 0)       | 5<br>(100)     | 0<br>( 0)             | 0<br>( 0)             |  |
|              | atrophy:turbinate                      | -<br>( -)                                                      | -<br>( -)         | -<br>( -)             | -<br>( -)             | 1<br>(20)       | 3<br>(60)      | 0<br>( 0)             | 0<br>( 0)             |  |
|              | ulcer:respiratory epithelium           | _<br>( -)                                                      | - ( -)            | -<br>( -)             | -<br>( -)             | 0<br>( 0)       | 2<br>(40)      | 0<br>( 0)             | 0<br>( 0)             |  |
|              | atrophy:olfactory epithelium           | -<br>( -)                                                      | -<br>( -)         | -<br>( -)             | -<br>()               | 0<br>( 0)       | 5<br>(100)     | 0<br>( 0)             | 0<br>( 0)             |  |
|              | erosion:respiratory epithelium         | -<br>( -)                                                      | ( -)              | ( -)                  | <br>()                | 2<br>( 40)      | 0<br>( 0)      | 0<br>( 0)             | 0<br>( 0)             |  |

Grade 1: Slight 2: Moderate 3: Marked 4: Severe

< a > a : Number of animals examined at the site

b b: Number of animals with lesion

(c) c:b/a\*100

(HPT150)

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PAGE : 2

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

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PAGE : 3

| Organ          | Findings                        | Group Name<br>No. of Animals on Study<br>Grade <u>1</u> (%) | 0<br>0<br><u>2 3 4</u><br>(%) (%) (%) | $ \begin{array}{c} 10 \text{ppm} \\ 0 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $ | $\begin{array}{c} 20 \text{ppm} \\ 0 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | 40ppm<br>0<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|----------------|---------------------------------|-------------------------------------------------------------|---------------------------------------|---------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------|-------------------------------------------------|
| [Respiratory : | svstem]                         |                                                             | -                                     |                                                                                                         |                                                                                                               |                                                 |
| nasal cavit    |                                 |                                                             | < 0>                                  | < 0>                                                                                                    | < 0>                                                                                                          | < 0>                                            |
|                | necrosis:respiratory epithelium | - ( -)                                                      | (-) (-) (-)                           | (-) (-) (-) (-)                                                                                         | (-) (-) (-) (-)                                                                                               | (-) (-) (-) (-)                                 |
| lung           |                                 |                                                             | < 0>                                  | < 0>                                                                                                    | < 0>                                                                                                          | < 0>                                            |
|                | congestion                      | -<br>( -) (                                                 | () () ()                              | < 0><br><br>( -) ( -) ( -) ( -)                                                                         | ( -) ( -) ( -) ( -)                                                                                           | ( -) ( -) ( -) ( -)                             |
| -              | edema                           | -<br>( -) (                                                 | ( -) ( -) ( -)                        | ( -) ( -) ( -) ( -)                                                                                     | ( -) ( -) ( -) ( -)                                                                                           | ( -) ( -) ( -) ( -)                             |
| [Hematopoieti  | c system]                       |                                                             |                                       |                                                                                                         |                                                                                                               |                                                 |
| thymus         | advanced a second               |                                                             | < 0>                                  | < 0>                                                                                                    | < 0>                                                                                                          | < 0>                                            |
|                | atrophy                         | ( -)                                                        | ( -) ( -) ( -)                        | ( -) ( -) ( -) ( -)                                                                                     | ( -) ( -) ( -) ( -)                                                                                           | ( -) ( -) ( -) ( -)                             |
| spleen         |                                 |                                                             | < 0>                                  | < 0>                                                                                                    | < 0>                                                                                                          | < 0>                                            |
|                | deposit of hemosiderin          | -<br>( -)                                                   | ( -) ( -) ( -)                        | (-) (-) (-) (-)                                                                                         | < 0><br>                                                                                                      | ( -) ( -) ( -) ( -)                             |
| Endocrine sy   | stem]                           |                                                             |                                       |                                                                                                         |                                                                                                               |                                                 |
| adrenal        |                                 |                                                             | < 0>                                  | < 0>                                                                                                    | < 0>                                                                                                          | < 0>                                            |
|                | congestion                      | ( -)                                                        | ( -) ( -) ( -)                        | ( -) ( -) ( -) ( -)                                                                                     | ( -) ( -) ( -) ( -)                                                                                           | ( -) ( -) ( -) ( -)                             |

(c) c:b/a\*100

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

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PAGE: 4

| Findings                        | No. of Animals on Study 0<br>Grade 1 2                                                                              | 3 4 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 160ppm<br>5<br><u>2 3 4</u><br>(%) (%) (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|---------------------------------|---------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------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| system]                         |                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                    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                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| necrosis:respiratory epithelium | < 0><br>                                                                                                            | 0<br>-) ( -) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | < 5><br>1 0 0<br>( 20) ( 0) ( 0)                                                                                                                                                                                                                                                                   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                                                                                          |
| consestion                      | < 0><br>                                                                                                            | 5<br>-) ( -) (100)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | < 5><br>0 0 0<br>( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                    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| edema                           |                                                                                                                     | 4<br>-) ( -) ( 80)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 0 0 0<br>( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                            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| c system]                       |                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                    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                                                                                          |
| atrophy                         | < 0><br>( -) ( -) (                                                                                                 | 0<br>-)(-)(0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | <pre> &lt; 4&gt;     1 0 0     ( 25) ( 0) ( 0)</pre>                                                                                                                                                                                                                                               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                                                                                          |
| deposit of hemosiderin          | < 0><br>( -) ( -) (                                                                                                 | 1<br>-) ( -) ( 20)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | < 5><br>0 0 0<br>( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                    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                                                                                          |
| stem]                           |                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                    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                                                                                          |
| congestion                      | < 0><br>                                                                                                            | 5<br>-) ( -) (100)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | <pre> &lt; 5&gt;<br/>0 0 0<br/>( 0) ( 0) ( 0)</pre>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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                                                                                          |
|                                 | system]<br>necrosis:respiratory epithelium<br>congestion<br>edema<br>cosystem]<br>atrophy<br>deposit of hemosiderin | No. of Animals on Study       0         Grade $\frac{1}{2}$ grade $\frac{1}{3}$ system]       (-) (-) (-) (         necrosis:respiratory epithelium       (-) (-) (         (-) (-) (-) (       (-) (-) (         congestion       (-) (-) (         edema       (-) (-) (         atrophy       (-) (-) (         (-) (-) (       (-) (         deposit of hemosider in       (-) (-) (         stem]       (-) (-) (         congestion       (-) (-) (         (-) (-) (       (-) (         deposit of hemosider in       (-) (-) (         stem]       (-) (-) (-) ( | No. of Animals on Study       0       1       2       3       4       1         Findines       1       2       3       4       1       1         system] $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ system] $     0$ consection $    0$ $0$ consection $       0$ $0$ edema $       0$ $0$ edema $      0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ <td< td=""><td>No. of Animals on Study       0       5         Findings       1       2       3       4       1       2       3       4         reade       1       2       3       4       1       2       3       4         accession       <math>(3)</math> <math>(3)</math><td>No. of Animals on Study       0       5         Findings       1       2       3       4       1       2       3       4         Findings       1       2       3       4       1       2       3       4         Sector       1       2       3       4       1       2       3       4         Sector       1       2       3       4       1       2       3       4         Sector       1       2       3       4       1       2       3       4         Sector       1       2       3       4       1       2       3       4         system       1       2       3       4       1       2       3       4         system       1       2       3       4       1       2       3       4         system       1       2       3       4       1       1       2       1       1       2       1       1       1       2       1       1       1       1       1       1       1       1       1       1       1       1       1       1       1</td></td></td<> | No. of Animals on Study       0       5         Findings       1       2       3       4       1       2       3       4         reade       1       2       3       4       1       2       3       4         accession $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ $(3)$ <td>No. of Animals on Study       0       5         Findings       1       2       3       4       1       2       3       4         Findings       1       2       3       4       1       2       3       4         Sector       1       2       3       4       1       2       3       4         Sector       1       2       3       4       1       2       3       4         Sector       1       2       3       4       1       2       3       4         Sector       1       2       3       4       1       2       3       4         system       1       2       3       4       1       2       3       4         system       1       2       3       4       1       2       3       4         system       1       2       3       4       1       1       2       1       1       2       1       1       1       2       1       1       1       1       1       1       1       1       1       1       1       1       1       1       1</td> | No. of Animals on Study       0       5         Findings       1       2       3       4       1       2       3       4         Findings       1       2       3       4       1       2       3       4         Sector       1       2       3       4       1       2       3       4         Sector       1       2       3       4       1       2       3       4         Sector       1       2       3       4       1       2       3       4         Sector       1       2       3       4       1       2       3       4         system       1       2       3       4       1       2       3       4         system       1       2       3       4       1       2       3       4         system       1       2       3       4       1       1       2       1       1       2       1       1       1       2       1       1       1       1       1       1       1       1       1       1       1       1       1       1       1 |

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

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| 0rgan                      | N                                                                                                                          | Coup Name         Oppm           p. of Animals on Study         0           rade         1         2         3         4           (%)         (%)         (%)         (%) | $ \begin{array}{c}     10ppm \\     0 \\     \frac{1  2  3  4}{(\%)  (\%)  (\%)  (\%)} \end{array} $ | $\begin{array}{c} & 20 \text{ppm} \\ 0 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | 40ppm<br>0<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|----------------------------|----------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|-------------------------------------------------|
| [Reproductive              | a system]                                                                                                                  |                                                                                                                                                                            |                                                                                                      |                                                                                                                 |                                                 |
| testis                     | germ cell necrosis                                                                                                         | <pre> &lt; 0&gt; ( -) ( -) ( -) ( -)</pre>                                                                                                                                 | < 0><br>                                                                                             | < 0><br><br>( -) ( -) ( -) ( -)                                                                                 | < 0><br>                                        |
| epididymis                 | decreased:sperma                                                                                                           | < 0><br><br>( -) ( -) ( -) ( -)                                                                                                                                            | < 0><br>                                                                                             | < 0><br><br>( -) ( -) ( -) ( -)                                                                                 | < 0><br><br>( -) ( -) ( -) ( -)                 |
|                            | debris of spermatic elements                                                                                               | ( -) ( -) ( -) ( -)                                                                                                                                                        | ( -) ( -) ( -) ( -)                                                                                  | ( -) ( -) ( -) ( -)                                                                                             | ( -) ( -) ( -) ( -)                             |
| (Nervous syst              | tem]                                                                                                                       |                                                                                                                                                                            |                                                                                                      |                                                                                                                 |                                                 |
| brain                      | degeneration:granular cell                                                                                                 | < 0><br>                                                                                                                                                                   | < 0><br>                                                                                             | < 0><br>                                                                                                        | < 0><br>                                        |
| 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 | Marked 4 : Severe<br>e                                                                                                                                                     |                                                                                                      |                                                                                                                 |                                                 |

(HPT150)

BAIS3

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

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PAGE: 6

| 0rgan                      |                                                                                                                                | μρ Name 80ppm<br>of Animals on Study 0<br>le <u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |  |
|----------------------------|--------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|-------------------------------------------------------|--|
| [Reproductive              | system]                                                                                                                        |                                                                                |                                                       |  |
| testis                     | germ cell necrosis                                                                                                             | < 0><br>( -) ( -) ( -) ( -)                                                    | < 5><br>4 0 0 0<br>( 80) ( 0) ( 0) ( 0)               |  |
| epididymis                 | decreased:sperma                                                                                                               | < 0><br>                                                                       | < 5><br>2 1 2 0<br>( 40) ( 20) ( 40) ( 0)             |  |
|                            | debris of spermatic elements                                                                                                   | ( -) ( -) ( -) ( -)                                                            | 2 3 0 0<br>(40)(60)(0)(0)                             |  |
| (Nervous syst              | em]                                                                                                                            |                                                                                |                                                       |  |
| brain                      | degeneration:granular cell                                                                                                     | < 0><br>                                                                       | < 5><br>0 3 0 0<br>( 0) ( 60) ( 0) ( 0)               |  |
| Grade<br>< a ><br>b<br>(c) | 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 | irked 4 : Severe                                                               |                                                       |  |

(HPT150)

BAIS3

# APPENDIX J 2

### HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE: SACRIFICED ANIMALS

(13 - WEEK STUDY)

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

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

| 0 <del>rgan</del> |                                        | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | 10<br>2<br>(%)      | 0ppm<br>3<br>(%) | <u>4</u><br>(%) | <u>1</u><br>(%) | 10<br>2<br>(%)    | 10pp<br>3<br>(%) | m<br>4<br>(%) | 1(%)      | 2<br>(%)  | 20<br>10<br>3<br>(%) | )ppm<br>4<br>(%) | - | 1<br>(%)   | 1(<br>2<br>(%) |           | ppm<br>4<br>(%) |   |
|-------------------|----------------------------------------|----------------------------------------------------------------|---------------------|------------------|-----------------|-----------------|-------------------|------------------|---------------|-----------|-----------|----------------------|------------------|---|------------|----------------|-----------|-----------------|---|
| [Respiratory :    | system]                                |                                                                |                     |                  |                 |                 |                   |                  |               |           |           |                      |                  |   |            |                |           |                 |   |
| nasal cavit       | inflammatory infiltration              | 0<br>( 0)                                                      | <10><br>0<br>( 0) ( | 0                | 0<br>0)         | 0<br>( 0) (     | <10><br>0<br>0) ( | 0                | 0<br>0)       | 0<br>( 0) | 0         | 10><br>0<br>( 0)     | 0<br>( 0)        |   | 0<br>0) (  | <1(<br>0<br>0) | 0         | 0<br>( 0)       |   |
|                   | erosion:squamous epithelium            | 0<br>( 0)                                                      | 0<br>( 0) (         | 0<br>0) (        | 0<br>0)         | 0<br>( 0) (     | 0<br>0) (         | 0<br>0) (        | 0<br>0)       | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)            | 0<br>( 0)        | ( | 0<br>0) (  | 0<br>0)        | 0<br>( 0) | 0<br>( 0)       |   |
|                   | respiratory metaplasia:olfactory epith | elium 0<br>(0)                                                 | 0<br>( 0) (         | 0<br>0) (        | 0<br>0)         | 0<br>( 0) (     | 0<br>0) (         | 0<br>0) (        | 0<br>0)       | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)            | 0<br>( 0)        |   | 0<br>0) (  | 0<br>0)        | 0<br>( 0) | 0<br>( 0)       |   |
|                   | squamous cell metaplasia:respiratory e |                                                                | 0<br>( 0) (         | 0<br>0) (        | 0<br>0)         | 0<br>( 0) (     | 0<br>0) (         | 0<br>0) (        | 0<br>0)       | 4<br>(40) | 0<br>( 0) | 0<br>( 0)            | 0<br>( 0)        |   | 9<br>30) ( | 1<br>10)       | 0<br>( 0) | 0 *<br>( 0)     | * |
|                   | atrophy:turbinate                      | 0<br>( 0)                                                      | 0<br>( 0) (         | 0<br>0) (        | 0<br>0)         | 0<br>( 0) (     | 0<br>0) (         | 0<br>0) (        | 0<br>0)       | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)            | 0<br>( 0)        |   | 0<br>0) (  | 0<br>0)        | 0<br>( 0) | 0<br>( 0)       |   |
|                   | ulcer:olfactory epithelium             | 0<br>( 0)                                                      | 0<br>( 0) (         | 0<br>0) (        | 0<br>0)         | 0<br>( 0) (     | 0<br>0) (         | 0<br>0) (        | 0<br>0)       | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)            | 0<br>( 0)        |   | 0<br>0) (  | 0<br>0)        | 0(0)      | 0<br>( 0)       |   |
|                   | atrophy:olfactory epithelium           | 0<br>( 0)                                                      | 0<br>( 0) (         | 0<br>0) (        | 0<br>0)         | 0<br>( 0) (     | 0<br>0) (         | 0<br>0) (        | 0<br>0)       | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)            | 0<br>( 0)        |   | 0<br>0) (  | 0<br>0)        | 0<br>( 0) | 0<br>( 0)       |   |
|                   | erosion:respiratory epithelium         | 0<br>( 0)                                                      | 0<br>( 0) (         | 0<br>0) (        | 0<br>0)         | 0<br>( 0) (     | 0<br>0) (         | 0<br>0) (        | 0<br>0)       | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)            | 0<br>( 0)        |   | 0<br>0) (  | 0<br>0)        | 0<br>( 0) | 0<br>( 0)       |   |

Grade 1: Slight 2: Moderate 3: Marked 4: Severe

< a > a : Number of animals examined at the site

b b: Number of animals with lesion

(c) c:b/a\*100

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

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

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PAGE : 2

0rgan	Findines	Group Name No. of Animals on Study Grade <u>1</u> (%)	10 2	80ppm <u>3</u> (%)	<u>4</u> (%)	<u>1</u> (%)	5 2	160ppn <u>3</u> (%)	n <u>4</u> (%)	
[Respiratory s	ystem]									
nasal cavit	inflammatory infiltration	5 (50)	<10> 5 (50) (0	0 ** 0)		< 5> 3 60) (0		
	erosion:squamous epithelium	0 (0)	0 (0) (0 0) (0 0)	1 (20) (0 0) (0 0) (0 0)	
	respiratory metaplasia:olfactory epi		1 (10) (0 0) (0 0)	1 (20) (
	squamous cell metaplasia:respiratory		10 (100) (0 0) (0 ** 0)	0 (0) (1		0 0) (0 ** 0)	
	atrophy:turbinate	10 (100)	0 (0) (0 0) (0 ** 0)	3 (60) (0 0) (0 ** 0)	
	ulcer:olfactory epithelium	2 (20)	0 (0) (0 0) (0 0)	0 (0) (0 0) (0 0)	
	atrophy:olfactory epithelium		10 (100) (0 0) (0 ** 0)	2 (40) (0 0) (
	erosion:respiratory epithelium	4 (40)	0 (0) (0 0)	1 (20) (0 0) (0 0)	

Grade 1: Slight 2: Moderate 3: Marked 4: Severe

< a > a : Number of animals examined at the site

b b: Number of animals with lesion

(c) c:b/a*100

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

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

0rgan	_ Findings	Group Name Oppm No. of Animals on Study 10 Grade 1 2 3 4 (%) (%) (%) (%)	$ \begin{array}{c} 10 \\ 10 \\ \frac{1}{(\%)} \\ (\%) \\ $	$ \begin{array}{c} 20ppm \\ 10 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$ \begin{array}{c} 40 \text{ppm} \\ 10 \\ \frac{1}{(\%)} (\%) (\%) (\%) \end{array} $
[Respirator	y system]				
lung	edema	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
[Hematopoie	otic system]				
spleen	deposit of hemosiderin	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
	extramedullary hematopoiesis	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0)(0)(0)(0)(0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
[Digestive	system]				
liver	herniation	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 1 0 0 0 (10) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
(Urinary sy	rstem]				

kidney	<10>	<10>	<10>	<10>
eosinophilic body	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	10 0 0 0 (100) (0) (0) (0)	10 0 0 0 (100) (0) (0) (0)	10 0 0 0 (100) (0) (0) (0)

Grade 1: Slight 2: Moderate 3: Marked 4: Severe

< a > a : Number of animals examined at the site

b b: Number of animals with lesion

(c) c:b/a*100

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

PAGE : 3

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

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PAGE : 3

0rgan	Group No. of Grade _ Findings	Name Oppm ¹ Animals on Study 10 <u>1 2 3 4</u> (%) (%) (%) (%)	$ \begin{array}{c} 10 \\ 10 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$ \begin{array}{c} 20 \text{ppm} \\ 10 \\ \underline{1 2 3 4} \\ (\%) (\%) (\%) (\%) (\%) \end{array} $	40ppm 10 <u>1 2 3 4</u> (%) (%) (%) (%)
[Respirator	י system]				
lung	edema	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
[Hematopoie	ətic system]				
spleen	deposit of hemosiderin	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
	extramedullary hematopoiesis	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
[Digestive	system]				
liver	herniation	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 1 0 0 0 (10) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
[Urinary sy	vstem]				
kidney	easinaphilic body	$\begin{array}{c} <10>\\ 10 & 0 & 0 \\ (100) & (& 0) & (& 0) \\ \end{array}$	<10> 10 0 0 0 (100) (0) (0) (0)	<10> 10 0 0 0 (100) (0) (0) (0)	<10> 10 0 0 0 (100) (0) (0) (0)
Grade < a > b (c) Significant	1: Slight2: Moderate3: Marka: Number of animals examined at the siteb: Number of animals with lesionc: b/a * 100t difference;*: P ≤ 0.05				

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

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PAGE: 4

0rgan	1	Group Name 80ppm No. of Animals on Study 10 Grade 1 2 3 4 (%) (%) (%) (%)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
[Respirator	y system]			
lung	edema	<10> 0 0 0 0 (0) (0) (0) (0)	< 5> 1 0 0 0 (20) (0) (0) (0)	
[Hematopoie	ptic system]			
spleen	deposit of hemosiderin	<10> 0 0 0 0 (0) (0) (0) (0)	< 5> 3 0 0 0 * (60) (0) (0) (0)	
	extramedullary hematopoiesis	0 0 0 0 (0) (0) (0) (0)	2 0 0 0 (40) (0) (0) (0)	
[Digestive	system]			
liver	herniation	<10> 0 0 0 0 (0) (0) (0) (0)	< 5> 0 0 0 0 (0) (0) (0) (0)	
[Urinary sy	/stem]			
kidney	eosinophilic body	<10> 10 0 0 0 (100) (0) (0) (0)	< 5> 3 0 0 0 (60) (0) (0) (0)	
Grade < a > b (c)	1: Slight 2: Moderate 3: a: Number of animals examined at the sit b: Number of animals with lesion c: b/a * 100	Marked 4 : Severe te		

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

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Organ	Findings	Group Name Oppm No. of Animals on Study 10 Grade 1 2 3 (%) (%) (%) (%)		$\begin{array}{c} 20 \text{ppm} \\ 10 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$	$\begin{array}{c} & 40 \text{ppm} \\ 10 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$
Endocrine sy	rstem]				
adrena l	micro vesicular fatty change	<10> 0 0 0 (0) (0) (0) (<10> 0 0 0 0 0 0) (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
Reproductive	9 system]				
estis	germ cell necrosis	<10> 0 0 0 (0) (0) (0) (<pre> <10> 0 0 0 0 0 0) (0) (0) (0) (0)</pre>	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
oididymis	decreased:sperma	<10> 0 0 0 (0) (0) (0) (<10> 0 0 0 0 0 0) (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
	debris of spermatic elements	0 0 0 (0) (0) (0) (0 0 0 0 0 0) (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
Nervous syst	em]				
rain	degeneration:granular cell	<10> 0 0 0 (0) (0) (0) (<pre> <10> 0 0 0 0 0 0) (0) (0) (0) (0)</pre>	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)

< a > a : Number of animals examined at the site

b b: Number of animals with lesion

(c) c:b/a*100

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

(HPT150)

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

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0rgan	N	roup Name 80ppm b. of Animals on Study 10 rade <u>1 2 3 4</u> (%) (%) (%) (%)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
[Endocrine sy	vstem]			
adrena l	micro vesicular fatty change	<10> 0 0 0 0 (0) (0) (0) (0)	< 5> 5 0 0 0 ** (100) (0) (0) (0)	
[Reproductive	ə system]			
testis	germ cell necrosis	$\begin{array}{c} <10 \\ 0 \\ (0) \\ (10) \\ (0 $	< 5> 0 3 2 0 ** (0) (60) (40) (0)	
epididymis	decreased:sperma	<10> 1 0 0 0 (10) (0) (0) (0)	< 5>	
	debris of spermatic elements	0 1 0 0 (0) (10) (0) (0)	2 3 0 0 ** (40) (60) (0) (0)	
(Nervous syst	tem]			
brain	degeneration:granular cell	<10> 0 0 0 0 (0) (0) (0) (0)	< 5> 1 3 0 0 ** (20) (60) (0) (0)	
Grade < a > b (c)	1: Slight2: Moderate3:a: Number of animals examined at the siteb: Number of animals with lesionc: b / a * 100difference; $*: P \leq 0.05$			

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

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		Group Name No. of Animals on Study	0ppm 10	10ppm 10	20ppm 10	40ppm 10
rgan	Findings	Grade <u>1</u> (%)	2 3 4 (%) (%) (%)	$\frac{1}{(\%)} \frac{2}{(\%)} \frac{3}{(\%)} \frac{4}{(\%)}$	$\frac{1}{(\%)} \frac{2}{(\%)} \frac{3}{(\%)} \frac{4}{(\%)}$	$\frac{1}{(\%)} \begin{array}{c} 2 & 3 & 4 \\ (\%) & (\%) & (\%) & (\%) \end{array}$
Special sense o	rgans/appandage]					
larder gl	granulation	0 (0)	<10> 0 0 0 (0) (0) (0)	<10> 1 0 0 0 (10) (0) (0) (0)	<10> 1 0 0 0 (10) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
[Body cavities]						
nesenterium	foreign body granuloma	0 (0)	<10> 0 0 0 (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
(a) a b b (c) c	: Slight 2 : Moderate : Number of animals examined at 1 : Number of animals with lesion : b / a $*$ 100	3 : Marked 4 : Severe the site P ≦ 0.01 Test of Chi Squar				

(HPT150)

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

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PAGE: 8

0rgan	No.	Sup Name 80ppm . of Animals on Study 10 ade 1 2 3 4	160ppm 5 <u>1 2 3 4</u> (%) (%) (%) (%)	
[Special sens	se organs/appandage]			
Harder gl	granulation	<10> 0 0 0 0 (0) (0) (0) (0)	< 5> 0 0 0 0 (0) (0) (0) (0)	
[Body cavitio	es]			
mesenterium	foreign body granuloma	<10> 1 0 0 0 (10) (0) (0) (0)	< 5> 0 0 0 0 (0) (0) (0) (0)	
Grade < a > b (c) Significant o	1: Slight2: Moderate3: Notesta: Number of animals examined at the siteb: Number of animals with lesionc: b / a * 100difference;*: P ≤ 0.05	Narked 4 : Severe 01 Test of Chi Square		
(HPT150)				 ВАІ

(13 - WEEK STUDY)

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

APPENDIX J 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

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

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PAGE	:	7
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0rgan	No	roup Name 0p 0. of Animals on Study 0 rade <u>1 2 3</u> (%) (%) (%)	$\begin{array}{c} 10 \text{ppm} & 0 \\ \hline 0 & 1 \\ \hline \frac{4}{(\%)} & \frac{1}{(\%)} & \frac{2}{(\%)} & \frac{3}{(\%)} \\ \hline \end{array}$	$ \begin{array}{c} 20 \text{ppm} \\ 0 \\ \underline{1 2 3 4} \\ \underline{(\%) (\%) (\%) (\%)} \end{array} $	40ppm 0 <u>1 2 3 4</u> (%) (%) (%) (%)
[Respiratory	system]				
nasal cavit	achesion	< 0> (-) (-) (-)	(-) (-) (-) (-)	< 0> 	< 0>
	inflammatory infiltration	(-) (-) (-)	() (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
	respiratory metaplasia:olfactory epithe	.ium – – – – (–) (–) (–)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
	squamous cell metaplasia:respiratory ep	thelium	(-) (-) (-) (-)	 (-) (-) (-) (-)	 (-) (-) (-) (-)
	atrophy:turbinate	 (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
	ulcer:respiratory epithelium	(-) (-) (-)	(-) (-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
	atrophy:olfactory epithelium	(-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
	erosion:respiratory epithelium	() () ()	() (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)

< a > a : Number of animals examined at the site

b b: Number of animals with lesion

(c) c:b/a*100

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

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PAGE: 8

Organ		DUP Name 80ppm . of Animals on Study 0 ade <u>1 2 3 4</u> (%) (%) (%) (%)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
[Respiratory :	system]			
nasal cavit	adhesion	< 0> 	< 8> 0 1 0 0 (0) (13) (0) (0)	
	inflammatory infiltration	(-) (-) (-) (-)	2 4 0 0 (25)(50)(0)(0)	
	respiratory metaplasia:olfactory epithel		1 0 0 0 (13) (0) (0) (0)	
	squamous cell metaplasia:respiratory epi [.]	thelium	0 8 0 0 (0) (100) (0) (0)	
	atrophy:turbinate	(-) (-) (-) (-)	0 7 1 0 (0) (88) (13) (0)	
	ulcer:respiratory epithelium	(-) (-) (-) (-)	0 I I 0 (0) (13) (13) (0)	
	atrophy:olfactory epithelium	() () ()	0 8 0 0 (0) (100) (0) (0)	
	erosion:respiratory epithelium	(-) (-) (-) (-)	3 0 0 0 (38) (0) (0) (0)	

Grade 1: Slight 2: Moderate 3: Marked 4: Severe

< a > a : Number of animals examined at the site

b b: Number of animals with lesion

(c) c:b/a*100

Findings_

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

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Group Name 0ppm 10ppm No. of Animals on Study 0 0 0 Grade 2 3 3 2 4 2 4 - 1 (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%)

[Respiratory system]

0rgan_

nasal cavit		< 0>	< 0>	< 0>	< 0>
	necrosis:respiratory epithelium	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
lung	congestion	< 0>	< 0>	< 0>	< 0>
		(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
	edema		(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
	deposit of hemosiderin	() () ()	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)

[Homatopoietic system]

thymus	atrophy	< 0>	< 0>	< 0>	< 0>
spleen		(-) (-) (-) (-) < 0>	(-) (-) (-) (-) < 0>	(-) (-) (-) (-) < 0>	(-) (-) (-) (-) < 0>
	atrophy	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

<a>> a : Number of animals examined at the site

b b : Number of animals with lesion

(c) c:b/a*100

(HPT150)

BAIS3

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4

(%)

40ppm

3

(%)

0

2

(%)

(%)

20ppm

4

(%)

3

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

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0rgan	Findings	Group Name 80ppm No. of Animals on Study 0 Grade 1 2 3 4 (%) (%) (%) (%) (%)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
[Respiratory	system]			
nasal cavit	necrosis:respiratory epithelium	< 0> (-) (-) (-) (-)	< 8> 1 2 1 0 (13) (25) (13) (0)	
lung	congestion	< 0> 	< 8> 7 0 0 0 (88) (0) (0) (0)	
	edema	(-) (-) (-) (-)	4 0 0 0 (50) (0) (0) (0)	
	deposit of hemosiderin	(-) (-) (-) (-)	1 0 0 0 (13) (0) (0) (0)	
[Hematopoieti	c system]			
thymus	atrophy	< 0> 	< 6> 0 5 0 0 (0) (83) (0) (0)	
spleen	atrophy	< 0> (-) (-) (-) (-)	< 8> 1 0 0 0 (13) (0) (0) (0)	

(HPT150)

EPORT TYPE : EX :	AI FEMALE						PAGE
rgan	Findings	Group Name No. of Animals on Study Grade <u>1</u> (%)		$\begin{array}{c} 10;\\ 0\\ \frac{1}{(\%)}, (\%) \\ (\%) $	$\frac{4}{(\%)} \qquad \frac{1}{(\%)}$	20ppm 0 2 3 4 (%) (%) (%)	40ppm 0 <u>1 2 3 4</u> (%) (%) (%) (%)
lematopoieti	c system]						
pleen	deposit of hemosiderin	- (-) (< 0> (-) (-)		(-) (-)	< 0> (-) (-) (-)	< 0> (-) (-) (-) (-)
rinary syst	em]						
in bladd	dilatation	- (-) (< 0> () (_) (-) (-) (-) (-)	()	< 0> (-) (-) (-)	< 0> (-) (-) (-) (-)
ervous syst	em]						
ain	degeneration:granular cell	_ (_) (< 0> 	< 0> -) (-) (-) (-)	(-) (-)	< 0> () () ()	< 0>
ade a > b c)	1: Slight 2: Moderate a: Number of animals examined at the b: Number of animals with lesion c: b / a * 100	3:Marked 4:Severe e site					

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REPORT TYPE	: RAT F344/DuCrj	HISTOLOGICAL FINDINGS :NON- DEAD AND MORIBUND ANIMALS ((PAGE : 12
0rgan	Findings	Group Name 80ppm No. of Animals on Study 0 Grade $\frac{1 \ 2 \ 3 \ 4}{(\%) \ (\%) \ (\%) \ (\%)}$	160ppm 8 <u>1 2 3 4</u> (%) (%) (%) (%)	
[Hematopoiet	ic system]			
spleen	deposit of hemosiderin	< 0> (-) (-) (-) (-)	<pre></pre>	
(Urinary sys	tem]			
urin bladd	dilatation	< 0> 	<pre></pre>	·
(Nervous sys	stem]			
brain	degeneration:granular cell	< 0> 	< 8> 0 5 3 0 (0) (63) (38) (0)	
Grade < a > b (c)	1: Slight 2: Moderate a: Number of animals examined at b: Number of animals with lesion c: b/a*100	3 : Marked 4 : Severe the site		

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(HPT150)

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APPENDIX J 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : SACRIFICED ANIMALS

(13 - WEEK STUDY)

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

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PAGE: 9

0rgan		Group Name No. of Animals on Study Grade <u>1</u> (%)	Oppm 10 <u>2 3 4</u> (%) (%) (%)	$ \begin{array}{c} 10 \text{ppm} \\ 10 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$ \begin{array}{c} 20 \text{ppm} \\ 10 \\ \underline{1 2 3 4} \\ (\%) (\%) (\%) (\%) \\ \end{array} $	40ppm 10 <u>1 2 3 4</u> (%) (%) (%) (%)
[Respiratory s	system]				· · · ·	
nasal cavit	inflammatory infiltration	0 (0)	<10> 0 0 0 (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
	squamous cell metaplasia:respiratory o		0 0 0 (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	7 0 0 0 ** (70) (0) (0) (0)
	squamous cell metaplasia:olfactory ep		0 0 0 (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
	atrophy:turbinate	0 (0)	0 0 0 (0)(0)(0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
	atrophy:olfactory epithelium	0 (0)	0 0 0 (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
	erosion:respiratory epithelium	0 (0)	0 0 0 (0)(0)(0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
(Hematopoietic	system]					
bone marrow	granulation .	3 (30)	<10> 0 0 0 (0) (0) (0)	$\begin{array}{c} <10>\\ 2 & 0 & 0 & 0\\ (20) & (0) & (0) & (0) \end{array}$	<10> 1 0 0 0 (10) (0) (0) (0)	<10> 2 0 0 0 (20) (0) (0) (0)
<a>b	1: Slight 2: Moderate 3 a: Number of animals examined at the s b: Number of animals with lesion c: b / a * 100	: Marked 4 : Severe ite				

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

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

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0rgan	No	roup Name 80ppm 5. of Animals on Study 10 rade <u>1 2 3 4</u> (%) (%) (%) (%)		
[Respiratory	system]			
nasal cavit	inflammatory infiltration	<10> 8 2 0 0 (80) (20) (0) (0)	<pre></pre>	
	squamous cell metaplasia:respiratory ep	ithelium 0 10 0 0 (0) (100) (0) (0)	*** 0 2 0 0 ?) (0) (100) (0) (0)	
	squamous cell metaplasia:olfactory epit	netium 1 0 0 0 (10)(0)(0)(0)		
	atrophy:turbinate	10 0 0 0 (100) (0) (0) (0	*** 0 2 0 0 ?) (0) (100) (0) (0)	
	atrophy:olfactory epithelium	1 2 0 0 (10) (20) (0) (0		
	erosion:respiratory epithelium	0 0 0 0 (0) (0) (0) (0	1 0 0 0 ? (50) (0) (0) (0)	
[Hematopoieti	c system]			
bone marrow	granulation	<10> 0 0 0 0 (0) (0) (0) (0		
Grade くa> b (c)	1: Slight 2: Moderate 3: a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100	Marked 4 : Severe		

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

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Organ	Findings	Group Name No. of Animals on Study Grade <u>1</u> (%)	Oppm 10 <u>2 3 4</u> (%) (%) (%)	10ppm 10 <u>1 2 3 4</u> (%) (%) (%) (%)	$ \begin{array}{c} 20 \text{ppm} \\ 10 \\ \underline{1 2 3 4} \\ (\%) (\%) (\%) (\%) (\%) \end{array} $	40ppm 10 <u>1 2 3 4</u> (%) (%) (%) (%)
[Hematopoie	tic system]					
spleen	deposit of hemosiderin	0 (0) (<10> 0 0 0 0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
	extramedullary hematopoiesis	0 (0) (0 0 0 0)(0)(0)	0 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 0 (0) (0) (0) (0)
(Digestive	system]					
liver	herniation		<10> 0 0 0 0) (0) (0)	$\begin{array}{c} <10>\\ 1 & 0 & 0 & 0\\ (10) & (0) & (0) & (0) \end{array}$	$\begin{array}{cccc} <10>\\ 1 & 0 & 0 & 0\\ (10) & (0) & (0) & (0) \end{array}$	<10> 1 0 0 0 (10) (0) (0) (0)
	epidermal cyst	0 (0) (0 0 0 0)(0)(0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	1 0 0 0 (10) (0) (0) (0)
[Urinary sy	stem]					
kidney	mineralization:cortex		<10> 0 0 0 0) (0) (0)	<10> 1 0 0 0 (10) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe <a>> a : Number of animals examined at the site

b: Number of animals with lesion b

(c) c:b/a*100

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

(HPT150)

BAIS3

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

0rgan	Findings	Group Name 80ppm No. of Animals on Study 10 Grade 1 2 3 4 (%) (%) (%) (%) (%)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
[Hematopoie	tic system]			
spleen	deposit of hemosiderin	<10> 0 0 0 0 (0) (0) (0) (0)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
	extramedullary hematopoiesis	1 0 0 0 (10) (0) (0) (0)	0 0 0 0 ? (0) (0) (0) (0)	
[Digestive :	system]			
Liver	herniation	<10> 3 0 0 0 (30) (0) (0) (0)	< 2> 0 0 0 0 ? (0) (0) (0) (0)	
	epidermal cyst	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 ? (0) (0) (0) (0)	
Urinary sy	stem]			
kidney	mineralization:cortex	<10> 0 0 0 0 (0) (0) (0) (0)	< 2> 0 0 0 0 ? (0) (0) (0) (0)	
-	1 : Slight2 : Moderatea : Number of animals examined atb : Number of animals with lesionc : b / a * 100difference ;* : $P \leq 0.05$ mificant test is not applied, because P			

(HPT150)

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PAGE : 12

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

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0rgan	Findings	Group Name No. of Animals on Study 10 Grade <u>1 2 3</u> (%) (%) (%)	$\frac{0}{3} \frac{4}{3} \frac{1}{(\%)}$	10ppm 10 <u>2 3 4</u> (%) (%) (%)	20ppm 10 <u>1 2 3 4</u> (%) (%) (%) (%)	40ppm 10 <u>1 2 3 4</u> (%) (%) (%) (%)
[Reproductiv	ve system]					
uterus	epidermal cyst	<10> 0 0 ((0) (0) (0)) 0 0))(0)(0)	<10> 0 0 0 (0) (0) (0)	<10> 1 0 0 0 (10) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
(Nervous sys	stem]					
brain	degeneration:granular cell	<10> 0 0 ((0) (0) (0)) 0 0)) (0) (0)	<10> 0 0 0 (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
[Special ser	nse organs/appandage]					
өуө	cataract	<10> 0 0 ((0) (0) (0)) 0 0))(0)(0)	<10> 0 0 0 (0) (0) (0)	$\begin{array}{cccc} <10>\\ 1 & 0 & 0 \\ (10) & (0) & (0) & (0) \end{array}$	<10> 0 0 0 0 (0) (0) (0) (0)
Harder gl	granulation	<10> 0 0 ((0) (0) (0)		<10> 0 0 0 (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
Grade < a > b (c)	1: Slight 2: Moderate a: Number of animals examined at th b: Number of animals with lesion c: b / a * 100					

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

(HPT150)

BAIS3

PAGE : 13

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

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0rgan	Findings	Group Name 80ppm No. of Animals on Study 10 Grade 1 2 3 4 (%) (%) (%) (%)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
[Reproductiv	ve system]			
uterus	epidermal cyst	$\begin{array}{cccc} <10> \\ 0 & 0 & 0 & 0 \\ (& 0) & (& 0) & (& 0) \\ \end{array}$	< 2> 0 0 0 0 ? (0) (0) (0) (0)	
[Nervous sys	stem]			
brain	degeneration:granular cell	$\begin{array}{cccc} <10> \\ 0 & 0 & 0 & 0 \\ (& 0) & (& 0) & (& 0) \\ \end{array}$	< 2> 0 0 2 0 ? (0) (0) (100) (0)	
[Special ser	nse organs/appandage]			
вув	cataract	$\begin{array}{cccc} <10> \\ 0 & 0 & 0 & 0 \\ (& 0) & (& 0) & (& 0) \\ \end{array}$	< 2> 0 0 0 0 ? (0) (0) (0) (0)	
Harder gl	granulation	$\begin{array}{c} <10>\\ 1 & 0 & 0 & 0\\ (10) & (0) & (0) & (0)\end{array}$	<pre> < 2> 0 0 0 0 ? (0) (0) (0) (0)</pre>	
	1 : Slight 2 : Moderate a : Number of animals examined at b : Number of animals with lesion c : b / a * 100 difference ; * : P ≤ 0.05 ** nificant test is not applied,because			

(HPT150)

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APPENDIX K 1

IDENTITY OF GLYCIDOL IN THE 13 - WEEK INHALATION STUDY

IDENTITY OF GLYCIDOL IN THE 13-WEEK INHALATION STUDY

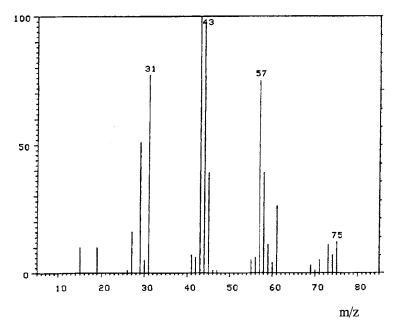
- A. Test Substance Lot No.: LER5803
- 1. Spectral data

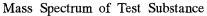
1

Mass Spectrometry

- Instrument : Hitachi M-80B Mass Spectrometer
- Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV





Determined Peak(m/z)	<u>Literature_Value</u> * Peak(m/z)
31	31
43	43
44	44
57	57
73	73
75	

Results: The mass spectrum was consistent with literature spectrum.

(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 1733)

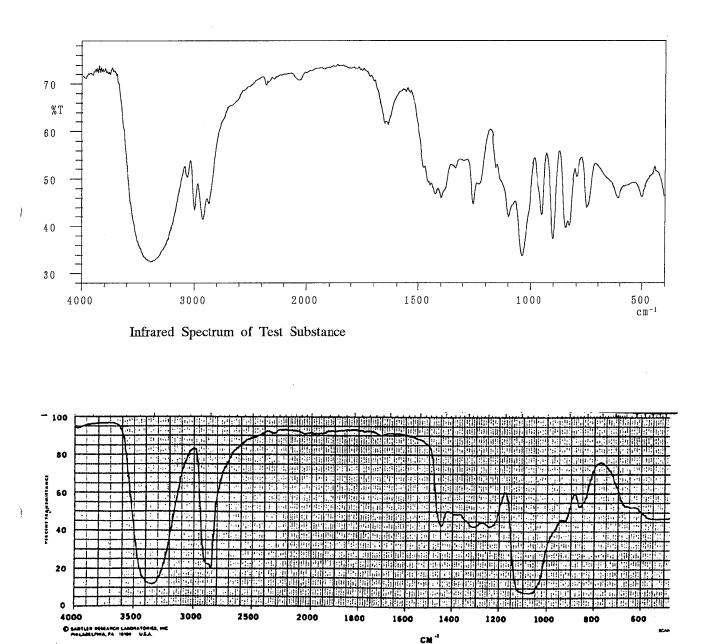
Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

 $: 4 \text{ cm}^{-1}$

Resolution



Infrared Spectrum of Glycidol (literature spectrum*)

Results: The infrared spectrum was consistent with literature spectrum.

(*William W. Simons (1978) The Sadtler Handbook of Infrared Spectra. Sadtler Research Laboratories, Inc. (U.K.), pp.480)

2. Conclusions: The result of the mass spectrum and the infrared spectrum agreed with the literature values. Consequently, the test substance was identified as glycidol.

- B. Test Substance Lot No.: LEQ5980
- 1. Spectral data

}

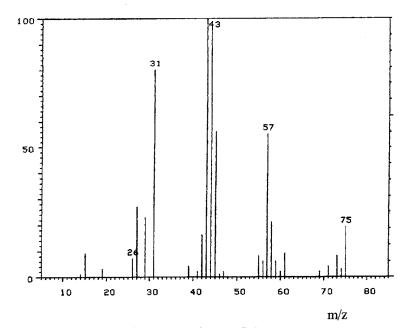
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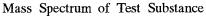
Mass Spectrometry

Instrument	: Hitachi	M-80B	Mass	Spectrometer
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Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV





Determined Peak(m/z)	Literature Value* Peak(m/z)
31	31
43	43
44	44
57	57
73	73
75	

Results: The mass spectrum was consistent with literature spectrum.

(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 1733)

Infrared Spectrometry

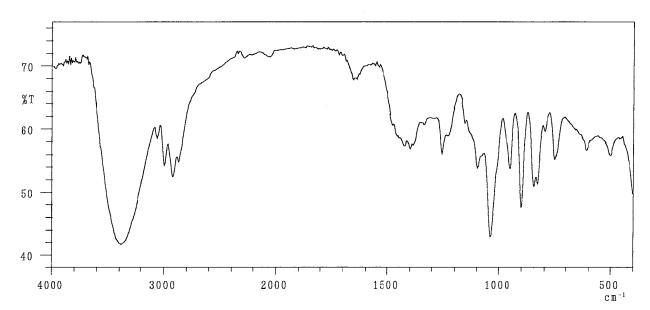
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

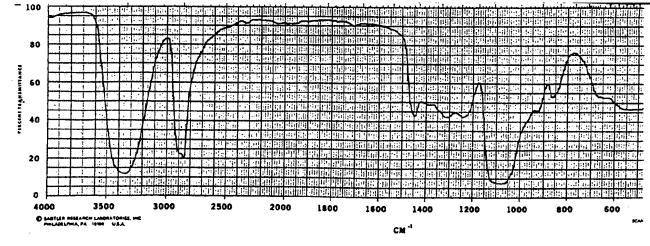
 $: 4 \text{ cm}^{-1}$

Resolution

)



Infrared Spectrum of Test Substance



Infrared Spectrum of Glycidol (literature spectrum*)

Results: The infrared spectrum was consistent with literature spectrum.

(*William W. Simons (1978) The Sadtler Handbook of Infrared Spectra. Sadtler Research Laboratories, Inc. (U.K.), pp.480)

2. Conclusions: The result of the mass spectrum and the infrared spectrum agreed with the literature values. Consequently, the test substance was identified as glycidol. APPENDIX K 2

STABILITY OF GLYCIDOL IN THE 13 - WEEK INHALATION STUDY

STABILITY OF GLYCIDOL IN THE 13-WEEK INHALATION STUDY

A. Test Substance Lot No.: LER5803

1.Sample: This lot was used from 1996.9.3 to 1996.10.14. Test substance was stored at room temperature.

2. Gas Chromatography

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Instrument	: Hewlett Packard 6890
Column	: Methyl Silicone (0.53 mm $\phi \times 60$ m)
Column Temperature	: 150°C
Flow Rate	: 10 mL/min
Detector	: FID (Flame Ionization Detector)
Injection Volume	: 1 µL

Results: Gas chromatography indicated one major peak (peak No.3) and two impurities (peak No.1,2 < 1% of total area) analyzed at 1996.8.30 and one major peak (peak No.3) and two impurities (peak No.1,2 < 1% of total area) analyzed at 1996.10.15. No new trace impurity peak in the test substance analyzed at 1996.10.15 was detected.

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
1996.08.30	1	1.89	0.15
	2	2.12	0.23
	3	2.52	99.62
1996.10.15	1	1.90	0.14
	2	2.13	0.23
	3	2.52	99.63

4. Conclusions: The results indicated that the test substance did not change when stored at room temperature during this period (for about 2 months).

B. Test Substance Lot No.: LEQ5980

1.Sample: This lot was used from 1996.10.15 to 1996.12.2. Test substance was stored at room temperature.

2. Gas Chromatography

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Instrument	: Hewlett Packard 6890
Column	: Methyl Silicone (0.53 mm $\phi \times 60$ m)
Column Temperature	: 150°C
Flow Rate	: 10 ml/min
Detector	: FID (Flame Ionization Detector)
Injection Volume	: 1 μL

Results: Gas chromatography indicated one major peak (peak No.3) and two impurities (peak No.1,2 < 1% of total area) analyzed at 1996.10.11 and one major peak (peak No.3) and two impurities (peak No.1,2 < 1% of total area) analyzed at 1996.12.11. No new trace impurity peak in the test substance analyzed at 1996.12.11 was detected.

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
1996.10.11	1	1.82	0.14
	2	2.12	0.23
	3	2.52	99.63
.996.12.11	1	1.89	0.14
	2	2.12	0.23
	3	2.52	99.63

4. Conclusions: The results indicated that the test substance did not change when stored at room temperature during this period (for about 2 months).

APPENDIX L 1

CONCENTRATION OF GLYCIDL IN THE INHALATION CHAMBER OF THE 13-WEEK INHALATION STUDY

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Group Name	Concentration(ppm) Mean \pm S.D.	
Control	0.0 ± 0.0	
10.0ppm	10.1 ± 0.1	
20.0ppm	19.8 ± 0.3	
40.0ppm	39.6 ± 0.6	
80.0ppm	79.8 ± 1.2	
160.0ppm	159.6 ± 2.4	

APPENDIX L 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13 - WEEK INHALATION STUDY OF GLYCIDOL

Group Name	Temperature (°C) Mean \pm S.D.	Humidity(%) Mean \pm S.D.	Ventilation Rate(L/min) Mean \pm S.D.	Air Change(time/h) Mean
Control	22.6 ± 0.1	55.5 ± 0.6	212.4 ± 1.1	12.0
25ppm	22.5 ± 0.1	56.6 ± 1.3	212.1 ± 1.1	12.0
50ppm	22.6 ± 0.1	55.6 ± 1.5	211.5 ± 1.3	12.0
100ppm	22.6 ± 0.1	54.5 ± 2.0	212.0 ± 1.1	12.0
200ppm	22.6 ± 0.2	54.5 ± 2.9	211.7 ± 1.1	12.0
400ppm	21.8 ± 0.2	53.3 ± 3.3	211.9 ± 1.1	12.0

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-WEEK INHALATION STUDY OF GLYCIDOL

APPENDIX M 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE 13 - WEEK INHALATION STUDY OF GLYCIDOL

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK INHALATION STUDY OF GLYCIDOL

Item	Method
Hematology	
Red blood cell (RBC)	Light scattering method ¹⁾
Hemoglobin (Hgb)	Cyanmethemoglobin method ¹⁾
Hematocrit (Hct)	Calculated as RBC \times MCV/10 ¹⁾
Mean corpuscular volume (MCV)	Light scattering method ¹⁾
Mean corpuscular hemoglobin (MCH)	Calculated as Hgb/RBC \times 10 ¹⁾
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as Hgb/Hct \times 100 ¹⁾
Platelet	Light scattering method ¹⁾
Reticulocyte	Pattern recognition method ³⁾
· · · · · · · · · · · · · · · · · · ·	(New methyleneblue staining)
Prothrombin time	Quick one stage method 2)
Activated partial thromboplastin time (APTT)	Ellagic acid activaterd method ²⁾
White blood cell (WBC)	Light scattering method ¹⁾
Differential WBC	Pattern recognition method ³⁾
	(May-Grunwald-Giemsa staining)
Biochemistry	
Total protein (TP)	Biuret method 4)
Albumin (Alb)	BCG method ⁴⁾
A/G ratio	Calculated as Alb/(TP-Alb) $^{4)}$
T-bilirubin	Alkaline azobilirubin method 4)
Glucose	Enzymatic method (GLK·G-6-PDH) 4)
T-cholesterol	Enzymatic method (CE·COD·POD) $^{4)}$
Triglyceride	Enzymatic method (LPL·GK·GPO·POD) ⁴⁾
Phospholipid	Enzymatic method (PLD·COD·POD)
Glutamic oxaloacetic transaminase (GOT)	$UV \cdot Rate method$
Glutamic pyruvic transaminase (GPT)	$UV \cdot Rate method$
Lactate dehydrogenase (LDH)	UV·Rate method ⁴⁾
Alkaline phosphatase (ALP)	p-Nitrophenylphosphate method ⁴⁾
γ -Glutamyl transpeptidase (γ -GTP)	L- γ -Glutamyl-p-nitroanilide method ⁴⁾
Creatine phosphokinase (CPK)	$UV \cdot Rate method$
Urea nitrogen	Enzymatic method (Urease · GLDH)
Creatinine	Jaffe method
Sodium	Ion selective electrode method ⁴⁾
Potassium	Ion selective electrode method ⁴⁾
Chloride	Ion selective electrode method ⁴⁾
Calcium	OCPC method
Inorganic phosphorus	Enzymatic method (PNP·XOD·POD)
Jrinalysis	5)
pH,Protein,Glucose,Ketone body,Bilirubin,Occult Blood,	Urinalysis reagent paper method
Urobilinogen	

1) Automatic blood cell analyzer (Technicon $H \cdot 1$: Technicon Instruments Corporation, USA)

2) Automatic coagulometer (Sysmex CA-5000 : Toa Medical Electronics Co.,Ltd.,Japan)

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

4) Automatic analyzer (Hitachi 7070 : Hitachi, Ltd., Japan)

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

APPENDIX M 2

UNITS AND DECIMARL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13 - WEEK INHALATION STUDY OF GLYCIDOL

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK INHALATION STUDY OF GLYCIDOL

Item	Unit	Decimal place
Hematology		
Red blood cell (RBC)	$\times 10^6 / \mu L$	2
Hemoglobin	g/dL	1
Hematocrit	%	1
Mean corpuscular volume (MCV)	fL	1
Mean corpuscular hemoglobin (MCH)	pg	1
Mean corpuscular hemoglobin concentration (MCHC)	g/dL	1
Platelet	\times 10 ³ / μ L	0
Reticulocyte	%	0
Prothrombin time	sec	1
Activated partial thromboplastin time (APTT)	sec	1
White blood cell (WBC)	$ imes$ 10 3 / μ L	2
Differential WBC	%	0
Biochemistry		
Total protein	g/dL	1
Albumin	g/dL	1
A/G ratio	-	1
T-bilirubin	mg/dL	2
Glucose	mg/dL	0
T-cholesterol	mg/dL	0
Triglyceride	mg/dL	0
Phospholipid	mg/dL	0
Glutamic oxaloacetic transaminase (GOT)	IU/L	0
Glutamic pyruvic transaminase (GPT)	IU/L	0
Lactate dehydrogenase (LDH)	IU/L	0
Alkaline phosphatase (ALP)	IU/L	0
γ -Glutamyl transpeptidase (γ -GTP)	IU/L	0
Creatine phosphokinase (CPK)	IU/L	0
Urea nitrogen	mg/dL	1
Creatinine	mg/dL	1
Sodium	mEq/L	0
Potassium	mEq/L	1
Chloride	mEq/L	0
Calcium	m mg/dL	1
Inorganic phosphorus	mg/dL	1

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