グリオキサルのラットを用いた経口投与による がん原性試験(混水試験)報告書

試験番号:0267

# APPENDIX

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## APPENDIX A 1

## CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(2-YEAR STUDY)

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : MALE

Clinical sign	Group Name	Administration Week-day													
		1-7	2-7	3–7	4-7	5-7	6-7	7-7	87	9-7	10-7	11-7	12-7	13-7	14-7
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ORIBUND SACRIFICE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
UNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PARALYTIC GAIT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EXCITEMENT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
MASTING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SOILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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28-7

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DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
MORIBUND SACRIFICE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PARALYTIC GAIT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EXCITEMENT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
WASTING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SOILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

SEX : MALE

Clinical sign

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

18-7

19-7

20-7

21-7

22-7

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17-7

Administration Week-day

16-7

15-7

Group Name

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23-7

24-7

25-7

26-7

27-7

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

SEX : MALE

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

PAGE : 3

Linical sign  EATH	Group Name	29–7	stration W 30-7	31-7	32-7	33-7	34-7	05 7	00 7	37-7	00.77	39-7	40-7	41-7	40.7
EATH					52-7	33-7	34-7	35-7	36~7	31-1	38-7	39-7	40-7	41-7	42-7
EATH															
	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DRIBUND SACRIFICE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
OCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
IUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PARALYTIC GAIT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	Ő	õ	Ō	Ō	Ō	Ó	Ō	Ō	õ	Ó	Ó	Ō	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	•0
XCITEMENT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	Ō	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	Ő	õ	ŏ	Ő	õ	ů 0	Ő	Ő	Ő	0	0	Ő	Õ
	3000 ppm	õ	õ	0	0	Ő	0	Ő	õ	Ő	õ	õ	õ	Ő	0
ASTING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	Ō	Ő	0	0	0	0	0	0	0	Ō	0	Ó	0
	1500 ppm	õ	0	ů	õ	õ	Ő	0	0	Õ	0 0	Ő	Ő	Ő	Õ
	3000 ppm	Ő	õ	Õ	õ	õ	Ő	0	Õ	Ő	Õ	Ő	õ	Ő	0
SOILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ō	õ	Ő	Õ	Ō	Ō	0	Õ	0	0	0	Ō	Ō	0
	1500 ppm	ŏ	õ	õ	ŏ	õ	õ	Õ	Õ	Õ	Õ	õ	õ	õ	ŏ
	3000 ppm	õ	õ	0	Õ	Õ	ů	Õ	Õ	Õ	Ő	Õ	0	ů	0

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Clinical sign	Group Name	Administration Week-day													
		43-7	44-7	45-7	46-7	47-7	48-7	49-7	50-7	51-7	52-7	53-7	54-7	55-7	56-7
										•			<u>^</u>		
EATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ORIBUND SACRIFICE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
IUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PARALYTIC GAIT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ó
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EXCITEMENT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0 .	0	0	0	0	0	0	0	0	0	0	0
WASTING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	Ō	0	0	0	0	Ő	Õ	Ő	Õ	Ő
	1500 ppm	Õ	0	Ő	õ	õ	Ő	õ	Ő	Ő	Ő	0 0	Ő	0	ŏ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ő
SOILED	Control	0	0	0	0	0	0	0	0	0	0	0	. 0	0	0
	750 ppm	Õ	Õ	Õ	Õ	õ	Õ	Õ	Õ	Ő	Õ	õ	Ő	õ	Ő
	1500 ppm	0	0	0	0	0	0	0	Ō	õ	Õ	Ō	Õ	õ	Ő
	3000 ppm	Ő	Ő	0	0	õ	Ő	õ	Ô	Ő	Ő	ñ	Ő	õ	ő

SEX : MALE

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

STUDY NO.	:	0267
ANIMAL	:	RAT F344/DuCrj
REPORT TYP	ΡĒ	: A1 104

SEX : MALE

linical sign	Group Name	Admin	istration 🛛	leek-day											
		57-7	58-7	59-7	60-7	61-7	62-7	63-7	64-7	65-7	66-7	67-7	68-7	69–7	70-7
EATH	Control	0	0	0	0	0	0	0	^	0	<u>^</u>	<u>^</u>		<u>^</u>	<u>,</u>
LATH	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0		0	1	1	1	1	1	1	1
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	1
		v	v	v	v	v	0	v	U	0	U	0	0	0	0
RIBUND SACRIFICE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	· 0	0	0	0	0	0	0	0	0
OCONOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	Ő	õ	Õ	Õ	õ	Ő	õ	õ	õ	Ő	0	0	Ő
	1500 ppm	õ	Õ	Õ	ŏ	ŏ	õ	Ő	õ	Ő	0 0	0	0	0 .	0
	3000 ppm	0	0	0	Ō	Ő	Ő	Ő	Õ	õ	0	Ő	ő	õ	ŏ
INCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0 0	Ő	0	0 0	õ	0	0	0	0	0	0	0	0	0
	1500 ppm	0	Ő	õ	0	Ő	0	0	0	0	0	0	0	0	0
	3000 ppm	0	ŏ	Ő	Õ	Ő	0	0	0	0	0	0	0	0	0
ARALYTIC GAIT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0 0	Ő	0	Ő	0	0 0	0	0	0	0	0	0	0	-
	1500 ppm	0	0	0	0	ŏ	0	0	0	0	0	0	0	0	0
	3000 ppm	Ő	0	0	0	Ő	0	0	0	0	0	0	0	0	0
								-	-	-	•	·	v	Ŭ	Ū
XCITEMENT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
STING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ō
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
)ILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	Ō	Ō	0	Ő	Ő	Ő	Ő	õ	0	0	Õ
	1500 ppm	0	Ō	Ō	Õ	Ő	Ő	õ	Ő	ů	õ	õ	0	0	0
	3000 ppm	0	Ō	Ō	Õ	Õ	Ő	ő	ů 0	ő	ŏ	Ő	õ	0	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : MALE

linical sign	Group Name	Admini	stration W	leek-day											· · · · ·
		71-7	72-7	73-7	74-7	75-7	76-7	77-7	787	79-7	80-7	81-7	82-7	83-7	84-7
* 6 1773															
EATH	Control	0	0	0	0	1	1	1	1	1	2	2	2	2	2
	750 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	1500 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	1	2	2
DRIBUND SACRIFICE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	1	1	1
	3000 ppm	0	0	0	0	0	0	0	0	0	õ	Ő	ō	ō	ō
OCOMOTOR MOVEMENT DECR	Control	0	0	0	1	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	Õ	0	0	Ő	Õ	0	0
	1500 ppm	0	0	0	0	0	Ō	Õ	Ő	0 0	0	ő	1	0	0
	3000 ppm	0	0	0	0	0	0	0	0	Ő	õ	õ	Ō	õ	õ
JNCHBACK POSITION	Control	0	0	0	1	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	Ó	Ő	ō	Ő	Õ	Ő	Ő	Ő	0	0	0	0	0
	1500 ppm	0	Õ	Õ	0	õ	Ö	0	0	Ő	0	0	0	0	•
	3000 ppm	0	Õ	0	0	0	0 0	0	0	0	0	0	0	0	0
ARALYTIC GAIT	Control	0	0	0	1	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	Ō	õ	ô	Ő	0	Ő	0	0	0	0	0	0	0
	1500 ppm	õ	Ő	õ	Ő	0	0	0	0	0	0	0		-	•
	3000 ppm	Ő	õ	Ő	õ	õ	0	0	0	0	0	0	0 0	0	0
XCITEMENT	Control	0	0	0	0	0	0	0	0	0	0	^	0	<u>^</u>	<u>^</u>
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	Ő	0	Ő	0	0	0	0		-	•	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		v	v	U	U	U	U	0	0	0	0	0	0	0	0
ASTING	Control	0	0	0	1	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	Ō	0	Ő	Ő	õ	Ő	Ő	0
	1500 ppm	0	0	0	0	0	0	Õ	õ	0	Ő	õ	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	Ő	Ő	0	Ő	Ő	0
OILED	Control	0	0	0	1	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	Ō	Ō	Õ	ŏ	õ	Ő	0	0	0	0	0	0
	1500 ppm	Õ	õ	Ő	Ő	õ	Ő	ŏ	0	0	0	0	0	0	0
	3000 ppm	0	0	Ō	õ	Ő	õ	ŏ	Ő	0	0	0	0	0	0

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\smile$ 

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SEX : MALE

Clinical sign	Group Name	Admini	stration W	leek-day											
		85-7	86-7	87-7	88-7	89-7	90-7	91-7	92–7	93-7	947	95-7	96-7	97-7	98-7
DEATH	Control	2	2	2	2	2	2	2	2	3	3	5	5	5	5
	750 ppm	1	2	2	2	2	2	3	3	3	3	3	3	4	5
	1500 ppm	1	1	1	1	1	1	1	2	3	3	3	3	3	3
	3000 ppm	2	2	2	2	2	2	3	3	3	3	3	3	3	3
ORIBUND SACRIFICE	Control	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	750 ppm	0	0	0	0	0	0	0	0	0	0	õ	ō	ō	Ô
	1500 ppm	1	1	1	1	1	1	1	1	1	1	1	1	2	2
	3000 ppm	0	Ō	ō	õ	0	ō	ō	ō	0	0	0	0	0	0
OCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	Ô	Ő	õ	Õ	Ő
	1500 ppm	0	0	0	0	0	Ō	Ō	Ō	Õ	Ő	Õ	Õ	ĩ	ŏ
	3000 ppm	0	0	0	0	0	õ	Ő	õ	õ	ŏ	0 0	0	0	0
UNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	Ö	0	Ő	õ
	1500 ppm	0	0	0	0	0	0	0	0	0	Ō	Õ	Õ	Õ	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	õ	Ő	Ő	0
PARALYTIC GAIT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ō
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	Ō	Õ	0
EXCITEMENT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	. 0	0	0	0	0	0	0	Õ
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ő	0
MASTING	Control	0	0	0	0	1	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Õ	õ	ŏ
	1500 ppm	0	0	0	0	0	0	0	0	Ō	ů	Ő	Õ	õ	Ő
	3000 ppm	0	0	0	0	0	0	0	0	Õ	Õ	Ő	0	õ	0
SOILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Ō	õ	Ő
	1500 ppm	0	0	0	0	0	0	0	0	0	Ō	Ő	Õ	Õ	ŏ
	3000 ppm	0	0	0	0	0	0	0	0	Ō	0	Ő	Õ	õ	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : MALE

Clinical sign Group Name Administration Week-day \_ 99-7 100-7 101-7 102-7 103-7 104-7 DEATH Control 750 ppm 1500 ppm 3000 ppm MORIBUND SACRIFICE Control 750 ppm 1500 ppm 3000 ppm LOCOMOTOR MOVEMENT DECR Control 750 ppm 1500 ppm 3000 ppm HUNCHBACK POSITION Control 750 ppm 1500 ppm 3000 ppm PARALYTIC GAIT Control 750 ppm 1500 ppm 3000 ppm EXCITEMENT Control 750 ppm 1500 ppm 3000 ppm WASTING Control 750 ppm 1500 ppm . 3000 ppm SOILED Control 750 ppm 1500 ppm 3000 ppm 

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS · \_\_\_\_

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SEX : MALE

Clinical sign	Group Name	Admini	stration We	ek-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	14-7
LAEDECTION	(control	•	0	<u>,</u>				_							·
ILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
OSS OF HAIR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ő	Õ
	3000 ppm	0	0	0	0	0	0	0	0	0	Ő	Ő	0 0	ő	õ
ROG BELLY	Control	0	0	0	0	0	0	0	0	0	0	0	ò	0	<u>^</u>
	750 ppm	ŏ	0	0 0	0	0	0	0	0			-	0	0	0
	1500 ppm	0	0	0	0	0	-	-	•	0	0	0	0	0	0
	3000 ppm	0	0	0			0	0	0	0	0	0	0	0	0
	JUVU PPM	U	U	U	0	0	0	0	0	0	0	0	0	0	0
SOILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Ō	0	Õ	Õ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ő	Ő
EYE HEMORRHAGIC DISCHA	Control	0	0	0	0	0	0	0	0	Ó	0	0	0	0	0
	750 ppm	0	Ō	0	Ő	õ	õ	Ő	õ	Ő	0	0	0	0	0
	1500 ppm	0	Õ	0	Ő	õ	õ	0	ŏ	ŏ	0	0	0	0	0
	3000 ppm	Ő	Õ	Ő	Ő	õ	õ	0	0	0	0	0	0	0	0
EVE OPACITY	Control	0	0	0	0	0	•								
CHE OFACITI	750 ppm		-	-	0	0	0	0	0	0	0	0	0	0	0
		0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CATARACT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	Ō	0	Õ	Ő	õ
	1500 ppm	0	0	0	0	0	0	Ō	õ	õ	õ	õ	0	0	0
	3000 ppm	0	0	0	0	0	0	Ő	Õ	õ	0	0	0	0	ŏ
CORNEAL OPACITY	Control	0	0	0	0	0	0	0	0	0	0	^	^	^	^
	750 ppm	ŏ	0	0	0	0	0	0	. 0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0					v	0	0	0	0
	3000 ppm	0	0	0	0		0	0	0	0	0	0	0	0	0
	SUUU PPM	v	U	U	v	0	0	0	0	0	0	0	0	0	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : MALE

Clinical sign	Group Name	Admini	istration W	eek-day											
		15-7	16-7	17-7	18-7	19–7	20-7	21-7	22–7	23-7	24-7	25-7	26-7	27-7	28-7
ILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DSS OF HAIR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ō
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ROG BELLY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	Ō	Ő	Ő	Õ	Õ
	1500 ppm	0	0	0	0	0	0	Ō	0	Ő	õ	Ő	Ő	0 0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	Ö	Ő	õ	0
DILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	Ó	0	0	0
	1500 ppm	0	0	0	0	0	0	Ō	Ő	Ő	Ô	Ő	õ	õ	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	õ	õ	0	Ő
YE HEMORRHAGIC DISCHA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	Ō	0	õ	õ	Ő	õ	0
	1500 ppm	0	0	0	0	Ō	Ő	Õ	Õ	ů 0	ů 0	õ	ŏ	0	0
	3000 ppm	0	0	0	0	0	0	0	0	Ő	0	0	Ő	Ő	Ő
YE OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ő	Õ	Õ	Õ	õ	õ	õ	0	0	0	0 0	0	0	0
	1500 ppm	Ő	õ	Õ	ŏ	õ	õ	õ	Ő	õ	0	Ő	0	0	0
	3000 ppm	Ő	õ	Ő	õ	Ő	õ	0	0	0	1	1	1	1	1
ATARACT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
· · · · · · · ·	750 ppm	0 0	õ	Ő	ŏ	0	0 0	ŏ	0	0	0	0	0	0	0
	1500 ppm	õ	0	ŏ	õ	0	0	0	0	0	0	0	0	0	0
	3000 ppm	Ő	ő	0	õ	õ	õ	0	0	õ	1	0 1	1	1	1
ORNEAL OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	ŏ	õ	ŏ	ŏ	ŏ	0	0	Ő	0	0	0	0	0	0
	1500 ppm	õ	Ő	õ	õ	0	0	0	0	0	0	0	0	0	0
	3000 ppm	õ	0	õ	ŏ	0	Ö	0	0	0	0	0	0	0	0
		v	v	v	v	v	v	U	U	U	U	U	U	U	0

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS -\_\_\_\_\_

SEX : MALE

Clinical sign	Group Name	Admini	istration W	eek-day											
		29-7	30-7	31-7	32-7	33-7	347	35-7	367	37-7	387	39-7	40-7	41-7	42-7
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
OSS OF HAIR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ROG BELLY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	Ő	Ő	Ö
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ő
SOILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EYE HEMORRHAGIC DISCHA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Ō	Ō	Ō	Õ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EYE OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	1	1	0	1	1	1	1	1	1	1	1	1	1
	1500 ppm	0	0	0	0	0	0	0	0	0	0	ō	0	Õ	ō
	3000 ppm	1	1	1	1	1	1	1	1	1	1	1	1	ĩ	1
CATARACT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	1	1	0	1	1	1	1	1	1	1	1	1	1
	1500 ppm	0	0	0	0	0	0	0	0	0	0	ō	õ	ō	Ō
	3000 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
CORNEAL OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	Ō	Õ	Ö	Ő	Ő	Ő	Ő	Ő
	1500 ppm	0	0	0	0	0	0	Ö	õ	Õ	õ	õ	0	0	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	Ő	Ő	Ő

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : MALE

Clinical sign	Group Name	Admini	stration W	eek-day						··	·				
		43-7	447	45-7	467	47-7	48-7	49-7	50-7	51-7	52-7	53-7	54-7	55-7	56-7
ILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	Ő	Ő	Ő	õ
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	õ	õ	õ
	3000 ppm	0	0 -	0	0	0	0	0	0	0	õ	Ő	Õ	Ő	0
OSS OF HAIR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ő	õ
	1500 ppm	0	0	0	0	0	0	0	Õ	Ő	õ	0	0 0	õ	0 0
	3000 ppm	0	0	0	0	Ō	Õ	Õ	õ	õ	õ	0	0	0	0
ROG BELLY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	Ō	õ	õ	Ő	õ	õ	0	0	0	0	0	0
	1500 ppm	Ō	Ō	õ	õ	Ő	ŏ	ŏ	ŏ	ŏ	0	0	0	0	0
	3000 ppm	0	0	Ő	Ő	Õ	0	õ	õ	0	0	0	0	0	0
OILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	Ó	0	õ	Ő	õ	õ	0 0	0	0	0	0	0
	1500 ppm	0	0	0	õ	ŏ	õ	õ	0 0	0	0	0	0		-
	3000 ppm	0	Ő	õ	Ő	Ő	Ő	0	0	0	0	0	0	0	0
YE HENORRHAGIC DISCHA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	Ō	0	Ő	õ	0	Ő	0	0
	1500 ppm	0	0	0	0	0	0	õ	Ő	ů	0	Ő	0	0	0
	3000 ppm	0	0	0	0	0	0	Ő	õ	Ő	Ő	0	0	0	Ő
YE OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	1	2	2	2	2	2	1	1	1	1	1	1	1	1
	1500 ppm	ō	õ	ō	0	0	0	0	1	1	2	2	1 2		-
	3000 ppm	1	1	1	1	1	1	1	1	1	2	2	2	2 2	2 2
ATARACT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	Δ
	750 ppm	1	1	1	1	1	1	1	1	1	1	1	•		0
	1500 ppm	0	Ô	0	0	0 0	0	0	1	1	1 2	1 2	1	1	1
	3000 ppm	1	1	1	1	1	1	1	1	1	2	2	2 1	2 1	2 1
ORNEAL OPACITY	Contral	0	0	0	0	0	0	0	0	0	0	^	^	•	^
	750 ppm	Ő	1	1	1	1	1	0	0	0	0	0	0	0	0
	1500 ppm	Ő	0	0	0	0	0	0	0	•	v	0	0	0	0
	3000 ppm	0	õ	0	0	0	0	0	0	0	0	0	0	0	0
		v	v	v	v	v	v	v	U	0	1	1	1	1	1

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS ·\_\_\_\_

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SEX : MALE

Clinical sign	Group Name	Admini	stration W	eek-dav											
		57-7	58-7	59-7	60-7	61-7	62-7	63-7	64-7	65-7	66-7	67-7	68-7	69-7	70-7
<u> </u>	· ····														
ILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ő
	1500 ppm	0	0	0	0	0	0	0	Ó	0	Ō	0	Ő	Ő	Ő
	3000 ppm	0	0	0	0	0	0	0	0	Ō	0	0	Õ	Ő	õ
OSS OF HAIR	Contral	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	Ō	0	0	0	õ	0	Ő
	1500 ppm	0	0	0	0	0	0	0	0	Õ	Ő	Õ	õ	0 0	ŏ
	3000 ppm	0	0	õ	0	õ	õ	õ	õ	0	0	0	0	0	0
FROG BELLY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	Õ	õ	Ő	Ő	õ	0	0	ŏ	Ő	0	0
	1500 ppm	ŏ	Ő	õ	Õ	Ő	0	Õ	0	0	0	0	0	0	-
	3000 ppm	Ő	Õ	0	0	0 0	õ	Ő	0	0	0	0	0	0	0
SOILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
	750 ppm	Ő	0	0	Ő	0	0	0			0	0	0	0	0
	1500 ppm	0	0	0	0				0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EYE HEMORRHAGIC DISCHA	Control	0	0	0	0	0	0	0	0	0	0	<u>^</u>			
ing individuality problem	750 ppm	0 0	0	0	0			-	0	0	0	0	0	0	0
	1500 ppm	0	0	0		0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		U	U	0	0	0	0	0	0	0	0	0	0	0	0
EYE OPACITY	Control	0	0	0	0	0	1	1	1	1	1	1	1	1	1
	750 ppm	1	1	1	1	1	1	2	2	2	2	2	2	2	2
	1500 ppm	3	3	3	3	3	3	3	3	3	3	3	3	3	3
	3000 ppm	2	2	2	2	2	2	2	2	2	2	2	2	2	2
ATARACT	Control	0	0	0	0	0	1	1	1	1	1	1	1	1	1
	750 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	1500 ppm	3	3	3	3	3	3	3	3	3	3	3	3	3	3
	3000 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
ORNEAL OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	1	1	1	1	1	ĩ	1	1
	1500 ppm	0	0	0	0	0	0	0	0	ō	ō	Ô	Ō	Ō	0
	3000 ppm	1	1	1	1	1	1	1	1	ĩ	1	1	1	1	1

SEX : MALE PAGE: 14 Clinical sign Group Name Administration Week-day 71-7 72~7 73-7 74-7 75-7 76-7 77--7 78-7 79-7 80-7 81-7 82-7 83-7 84-7 PILOERECTION Control 750 ppm 1500 ppm 3000 ppm LOSS OF HAIR Control 750 ppm 1500 ppm 3000 ppm FROG BELLY Control 750 ppm 1500 ppm 3000 ppm SOILED PERI GENITALIA Control 750 ppm 1500 ppm 3000 ppm EYE HEMORRHAGIC DISCHA Control 750 ppm 1500 ppm 3000 ppm EYE OPACITY Control 750 ppm 1500 ppm 3000 ppm CATARACT Control 750 ppm 1500 ppm з З 3000 ppm CORNEAL OPACITY Control 750 ppm 1500 ppm 3000 ppm 

CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\sim$ 

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SEX : MALE

Clinical sign	Group Name	Admin	istration W	eek-day												
		85-7	86-7	87-7	88-7	89-7	90-7	91-7	92-7	937	94-7	95-7	96-7	97-7	98-7	
PILOERECTION	Control	0	0	0	0	1	0	0	0	0	0	0	0	0	0	
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ö	
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ō	Ő	
LOSS OF HAIR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	750 ppm	0	0	0	0	0	0	0	0	0	0	Ō	0	Õ	õ	
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Õ	Ő	Ő	Ő	
	3000 ppm	0	1	1	1	1	1	1	1	1	1	1	1	ĩ	1	
FROG BELLY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	750 ppm	0	0	0	0	0	0	Ō	Ő	Õ	Õ	õ	Ő	õ	0	
	1500 ppm	0	0	0	Ō	õ	õ	ŏ	Ő	0	0	0	0	0	õ	
	3000 ppm	0	0	0	Õ	õ	Ő	Ő	õ	0	0	0	0	Ő	0	
SOILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	750 ppm	Ó	0	0	õ	õ	õ	õ	Ő	0	0	0	0	0	-	
	1500 ppm	Ö	õ	õ	õ	0	0	0	0	0	0	-		•	0	
	3000 ppm	Ő	0	0	Ő	0	0	0	0	0	0	0 0	0	0 0	0	
EYE HEMORRHAGIC DISCHA	Control	1	1	1	1	0	0	0	0	0	0	0	0	0	0	
	750 ppm	Ō	ō	ō	ō	Ő	õ	õ	0	0	0	0	0	0	-	
	1500 ppm	Ő	õ	õ	õ	0	õ	0 0	0	0	0	0		-	0	
	3000 ppm	Ő	0	Ö	õ	0	0	0	0	0	0	0	0	0 0	0 0	
EYE OPACITY	Contral	2	3	3	3	3	3	3	3	3	3	3	0	0		
	750 ppm	3	3	3 3	3	3	. 3	4	4	4	4	4	3 4	3 3	4	
	1500 ppm	3	3	3	3	3	3	4	4	4	4				3	
	3000 ppm	2	2	2	2	2	2	2	2	2	3 2	3 2	3 2	3 2	3	
CATARACT	Control	2	2	2	2	2	2	2	2	2	2	3	0	Ŷ	0	
-	750 ppm	2	2	2	2	2	2	3	3	4	4		3	3	3	
	1500 ppm	3	3	3	3	2 3	2	3 4	3 3	4 3	-	4	4	3	3	
	3000 ppm	2	2	2	2	2	2	42	3 2	3	3 2	3 2	3 2	3 2	3 2	
CORNEAL OPACITY	Control	0	1	1	1	1	1	1	1	1		•	^			
	750 ppm	1	1	1	1	1	1	1	-	1	1	0	0	0	0	
	1500 ppm	0	0	0	0	0	0		1	0	0	0	0	0	0	
	3000 ppm	0	. 0	0	0	0	0	0	0	0	0	0	0	0	0	
	anno hhili	v	. 0	U	v	v	U	U	0	0	0	0	0	0	0	

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\smile$ 

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SEX : MALE

Clinical sign	Group Name	Admin	istration	Week-day			
-		99-7	100-7	101-7	102-7	103-7	104-7
PILOERECTION	Control	0	0	0	0	1	0
	750 ppm	0	0	0	1	0	0
	1500 ppm	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0
LOSS OF HAIR	Control	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0
	1500 ppm	0	0	0	0	Õ	Ő
	3000 ppm	1	1	ů	õ	1	1
	PP01	-	-	~	v	-	1
FROG BELLY	Control	0	0	0	0	0	1
	750 ppm	0	0	0	0	0	
	1500 ppm	0	Ő	0	0		0
	3000 ppm	0	0	0	0	0	0
		v	v	U	U	0	0
SOILED PERI GENITALIA	Control	0	^	0		^	•
SOILLD TENT GENTIALIA	750 ppm	0	0		1	0	0
			0	0	0	0	0
	1500 ppm	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0
EYE HEMORRHAGIC DISCHA	Control	0	0	0	0	^	0
ETE BEROAMINGTO DISONA	750 ppm	0		-	-	0	0
	1500 ppm		0	0	0	0	0
		0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0
EYE OPACITY	Construct 1		-			•	•
EIE UFAGIII	Control	4	5	4	4	3	3
	750 ppm	3	3	3	3	3	3
	1500 ppm	3	2	2	2	2	2
	3000 ppm	2	2	3	3	3	3
C 1711 D 1 Cm		_					
CATARACT	Control	3	4	4	4	3	3
	750 ppm	3	3	3	3	3	3
	1500 ppm	3	2	2	2	2	2
	3000 ppm	2	2	3	3	3	3
	_						
CORNEAL OPACITY	Control	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0

(HAN190)

STUDY NO. :	0267
ANIMAL :	RAT F344/DuCrj
REPORT TYPE	: A1 104

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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REPORT TYPE : A1 104 SEX : MALE

Clinical sign	Group Name	Adminis	stration W	ek-day											
		1-7	27	3-7	4-7	5-7	6-7	7-7	8-7	9–7	107	11-7	12-7	13-7	14-7
ANTERIOS CHAMBER OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ABNORMAL GROWTH OF TEETH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	õ	õ	Ő
EXTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	Ö	0	Õ	0	õ	0
	1500 ppm	0	0	0	0	0	0	Ō	0	Ō	Õ	Õ	õ	0	õ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	õ	Ő	Ő
VTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Õ
	1500 ppm	0	0	0	0	0	0	0	0	Ő	Õ	0	0 0	Ő	õ
	3000 ppm	0	0	0	0	0	0	0	0	0	õ	Ő	õ	ů 0	Ő
N.PERI MOUTH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Õ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	Ő	Ő	Ő	Õ
M.ORAL CAVITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Õ	0
	1500 ppm	0	0	0	0	0	0	0	0	Ő	Õ	Õ	0	0	Ő
	3000 ppm	0	0	0	0	0	0	0	0	ő	õ	Ő	Ő	0	0
M.EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	Ō	Ō	Õ	Õ	0	Ő	Õ	0	Ő	Ô	0	Ő
	1500 ppm	Õ	Ő	õ	Ő	õ	õ	0 0	ŏ	0	0	. 0	0	0	0
	3000 ppm	0	0	Ő	õ	Ő	õ	0	õ	0	0	0	0	0	0
M.PERI EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	. 0
	750 ppm	õ	õ	0	Ő	0	0	0	0	0	0	0	0	0	0
	1500 ppm	Ő	õ	0	Ő	Ő	0	0	0	0	0	0	0		-
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		v	v	v	v	v	v	v	v	v	v	v	U	0	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\sim$ 

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SEX : MALE

Clinical sign	Group Name	Admin	istration 🖗	eek-day											
	·····	15-7	16-7	17-7	18-7	19-7	20-7	21-7	22-7	23-7	24-7	25-7	26-7	27-7	28-7
NTERIOS CHAMBER OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
BNORMAL GROWTH OF TEETH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ő	Õ
EXTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Õ	0
NTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Õ	Õ	õ
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Ő	õ	õ	õ
	3000 ppm	0	0	0	0	0	0	0	0	Ō	ō	õ	õ	õ	0
PERI MOUTH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ō	Ő
	1500 ppm	0	0	0	0	0	0	0	Ō	Ő	Ő	õ	õ	õ	õ
	3000 ppm	0	0	0	0	0	0	0	0	0	õ	õ	Õ	Ő	Ö
I.ORAL CAVITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	õ	Ő	Ő	Õ	ů
	1500 ppm	0	0	0	0	0	0	0	0	0	Õ	0 0	0	õ	0
	3000 ppm	0	0	0	0	0	0	0	Ő	õ	õ	0	0	0	0
I.EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	Ő	Õ	õ	õ	0	0	0	0	0	0
	1500 ppm	0	õ	õ	õ	õ	Ö	0	0	0 0	0	0	0	0	0
	3000 ppm	0	õ	Ő	õ	Ő	õ	õ	õ	0	0	0	0	0	0
I.PERI EAR	Control	0	0	0	0	0	0	0	0	0	٥	0	0	0	0
	750 ppm	0	Ō	Ő	Õ	Ő	0	õ	Ő	0	0	0	0	0	0
	1500 ppm	0	ō	õ	õ	ŏ	Õ	õ	0	0	0	0	0	0	0
	3000 ppm	Ő	0	õ	õ	Ő	õ	Ő	0	0	0	0	0	0	0

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104 CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : MALE

Linical sign G INTERIOS CHAMBER OPACITY INTERIOS CHAMBER OPACITY INTERNAL GROWTH OF TEETH EXTERNAL MASS	Group Name Control 750 ppm 1500 ppm 3000 ppm Control 750 ppm 1500 ppm 3000 ppm 1500 ppm 1500 ppm 1500 ppm 3000 ppm	29-7 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0	32-7 0 0 0 0 0 0	33-7 0 0 0 0	0 0 0 0 0	35-7 0 0 0 0	36-7 0 0 0	0 0 0	38-7 0 0 0	39-7 0 0 0	40-7 0 0 0	41-7 0 0 0	42-7 0 0
ABNORMAL GROWTH OF TEETH EXTERNAL MASS	750 ppm 1500 ppm 3000 ppm Cantral 750 ppm 1500 ppm 3000 ppm Cantral 750 ppm 1500 ppm	0 0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0	0 0 0	0	0	0 0	0	0	0	0	0	0
ABNORMAL GROWTH OF TEETH	750 ppm 1500 ppm 3000 ppm Cantral 750 ppm 1500 ppm 3000 ppm Cantral 750 ppm 1500 ppm	0 0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0	0 0 0	0	0	0 0	0	0	0	0	0	0
EXTERNAL MASS	1500 ppm 3000 ppm Cantral 750 ppm 1500 ppm 3000 ppm Cantral 750 ppm 1500 ppm		0 0 0 0	0 0 0 0	0 0 0	0 0	0	0	0		-				-
EXTERNAL MASS	3000 ppm Cantrol 750 ppm 1500 ppm 3000 ppm Cantrol 750 ppm 1500 ppm	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0	0		-	-	0	0	0	0	Δ.	
EXTERNAL MASS	Control 750 ppm 1500 ppm 3000 ppm Control 750 ppm 1500 ppm	0 0 0 0	0 0 0	0 0 0	0	-	0	0				-	-		0
XTERNAL MASS	750 ppm 1500 ppm 3000 ppm Control 750 ppm 1500 ppm	0 0 0	0	0	0	0		v	0	0	0	0	0	0	0
	1500 ppm 3000 ppm Control 750 ppm 1500 ppm	0	0	Õ	-		0	0	0	0	0	0	0	0	0
	1500 ppm 3000 ppm Control 750 ppm 1500 ppm	0	-	-		0	0	0	0	0	Ō	Ő	Õ	õ	Ő
	3000 ppm Control 750 ppm 1500 ppm	-	0	0	0	0	0	0	0	Ō	0	Õ	õ	õ	Ő
	750 ppm 1500 ppm	0		v	0	0	0	0	0	Ō	õ	Ő	Ö	õ	õ
	750 ppm 1500 ppm	v	0	0	0	0	0	0	0	0	0	0	0	0	0
NTERNAL MASS	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	-	0	0
NTERNAL MASS		0	0	0	0	0	0	0	0		•	0	0	0	0
NTERNAL MASS		0	0	0	0	0	0	0	0	0	0	-	0	0	0
NTERNAL MASS		U	v	U	U	U	U	U	U	0	U	0	0	0	0
	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
I.PERI MOUTH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Ő	õ	Ő
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Ō	Ō	Õ	Õ
	3000 ppm	0	0	0	0	0	0	0	0	0	Ő	Õ	õ	õ	Ő
I.ORAL CAVITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	•
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0		0	0
		v	v	v	v	U	v	v	v	v	U	U	0	0	0
I.EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Õ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
.PERI EAR	Control	0	0	0	. 0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ő	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	•	•
	3000 ppm	0	Ő	0	0	0	õ	0	0	0	0	0	0	0	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\sim$ 

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SEX : MALE

linical sign	Group Name	Admini	stration W	eek-dav											
		43-7	44-7	45-7	467	47-7	487	49-7	50-7	51-7	52-7	53-7	54-7	55-7	56-7
NTERIOS CHAMBER OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
BNORMAL GROWTH OF TEETH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
XTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	1	1	1	1	1
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ō
	1500 ppm	0	0	0	0	0	0	0	Ō	0	1	1	ĩ	1	1
	3000 ppm	0	0	0	0	0	0	0	0	0	ō	ō	1	1	1
TERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Ő	Ő	Ő
	1500 ppm	0	0	0	0	0	0	0	0	0	õ	õ	0	Ő	0
	3000 ppm	0	0	0	0	0	Ō	0	Ő	0	õ	0	ů 0	0	õ
.PERI MOUTH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	Ō	0	Õ	õ	Ő	0
	3000 ppm	0	0	0	0	0	0	0	0	õ	Ő	Ő	Ő	0	õ
.ORAL CAVITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	õ	0	õ	0 0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Õ	0 0	Ő	0
	3000 ppm	0	0	0	0	0	õ	ů	õ	Ő	Ő	õ	0	0	0
.EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Õ	0	õ	Ő	õ	Ő	õ	0	0	0	0	0	0	0
	1500 ppm	õ	õ	õ	0	õ	0	0	0	0	0	0	0	0	0
	3000 ppm	õ	0 0	õ	Ő	õ	0	0	0 0	0	0	0	0	0	0
.PERI EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	õ	õ	Ő	õ	ŏ	õ	0	Ö	0	0	0	0	0	0
	1500 ppm	0	õ	õ	Ő	0	Ő	0	0	0	0	0	0	•	0
	3000 ppm	ŏ	Ő	õ	0	Ő	0	0	0	0	0	0	0	0	0
		Ŭ	v	v	v	v	v	v	v	v	v	v	v	v	U

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\overline{\phantom{a}}$ 

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### SEX : MALE

inical sign	Group Name	AQIIIIII	stration W	еек-аау											
		57-7	58-7	59-7	60-7	61-7	62-7	63-7	64-7	65-7	66-7	67-7	68-7	69-7	70-7
NTERIOS CHAMBER OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
BNORMAL GROWTH OF TEETH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EXTERNAL MASS	Control	1	1	1	1	1	1	1	1	2	2	2	2	2	2
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	1	1	1	1	1	2	3	3	3	3	3	3	2	2
	3000 ppm	1	1	1	1	1	2	2	1	1	1	1	1	1	1
NTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	maa 0008	0	0	0	0	0	0	0	0	0	0	0	0	0	0
.PERI MOUTH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	1	1	1	1	1	1	1	1	1
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
I.ORAL CAVITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
I. EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ô
I.PERI EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	Ő	Ő	Ő	Ő
	1500 ppm	0	0	0	0	0	0	0	0	Ō	Ō	Õ	Õ	õ	Ő
	3000 ppm	0	0	Ó	0	0	0	0	0	0	Ő	Ő	õ	ŏ	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX	:	MALE

Clinical sign	Group Name	Admini	stration W	eek-day											
		71-7	72-7	73-7	74-7	757	76-7	77-7	78–7	79-7	80-7	81-7	82-7	83-7	84-7
NTERIOS CHAMBER OPACITY	Control	0	1	1	1	1	0	0	0	<u>^</u>	0	<u>^</u>			•
ATERIOS GIRIBER OF ROTTI	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	-	•	•	-	0	0	0	0	0
	3000 ppm	0	0	0	0		0	0	0	0	0	0	0	0	0
	2000 hhit	U	U	U	U	0	U	0	0	0	0	0	0	0	0
BNORMAL GROWTH OF TEETH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EXTERNAL MASS	Control	3	3	3	3	2	3	3	4	4	3	3	3	3	4
	750 ppm	õ	0	0	õ	0	0	0	0		0	0	1	J 1	4 3
	1500 ppm	3	3	3	3 3	2	2	2	3	3	3	3	3	-	
	3000 ppm	1	1	1	1	1	1	1	1	3 1	2	2	ა ვ	2 2	2
		1	T	1	I	1	1	1	1	1	2	2	3	2	2
NTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
I.PERI MOUTH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	Õ	Õ	õ	õ	0 0	õ	Ő
	1500 ppm	1	1	1	1	1	1	ĩ	1	1	1	1	1	1	1
	3000 ppm	ō	ō	õ	ō	ō	ō	0	ō	õ	Ō	0	0	0	0
								-		-	·	·	·	v	v
M.ORAL CAVITY	Control	0	0	0	0	. 0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M.EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	Ő	õ	õ	Õ	õ	Ő	õ	0	0	0	0
	1500 ppm	õ	õ	ŏ	õ	0	õ	0	õ	0	0	õ	0	0	0
	3000 ppm	0	Ō	Ő	õ	õ	Ő	0	õ	Ő	Ő	ŏ	0	0	0
DEDI END	Contro-1	٥	٥	0	0	0	0	0	•	0	•	0			
I.PERI EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	. 0
	750 ppm	0	U	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	1	1	Ţ	1	1	1	1	1	1	1	1	1	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\sim$ 

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SEX : MALE

Clinical sign	Group Name	Admini	stration W	eek-dav											
		85-7	86-7	87-7	88-7	89-7	90-7	91-7	92-7	93-7	94-7	95-7	96-7	97-7	98-7
NTERIOS CHAMBER OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SNORMAL GROWTH OF TEETH	Control	0	0	0	0	0	0	0	1	1	1	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
XTERNAL MASS	Control	4	5	5	5	5	5	5	5	4	4	4	4	4	4
	750 ppm	4	4	4	5	6	6	6	6	7	8	8	9	9	9
	1500 ppm	3	3	4	4	4	4	4	3	2	2	2	2	2	2
	3000 ppm	2	2	2	2	2	2	2	2	2	3	3	4	4	5
ITERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
.PERI MOUTH	Contral	0	0	0	1	1	1	1	1	0	0	1	1	1	1
	750 ppm	0	0	0	1	1	1	1	1	1	1	1	1	1	1
	1500 ppm	1	1	1	1	1	1	1	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
.ORAL CAVITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
.EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
.PERI EAR	Contral	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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### SEX : MALE

PAGE: 24

Clinical sign	Group Name	Admin	istration	leek-dav					
		99-7	100-7	101-7	102-7	103-7	104-7	 	···•
NTERIOS CHAMBER OPACITY	Contral	1	1	0	0	0	0		
	750 ppm	0	0	0	0	0	0		
	1500 ppm	0	0	0	0	0	0		
	3000 ppm	0	0	0	0	Ō	Ő		
NORMAL GROWTH OF TEETH	Control	0	0	0	0	0	0		
	750 ppm	ů 0	0	0	0	0	0		
	1500 ppm	0	Ő	0	0	0	0		
	3000 ppm	0	0	0	0	0			
	3000 ppm	U	U	U	0	0	0		
EXTERNAL MASS	Control	4	5	6	6	7	7		
	750 ppm	10	11	10	11	11	12		
	1500 ppm	2	1	2	2	2	2		
	3000 ppm	5	5	6	6	6	6		
INTERNAL MASS	Control	0	2	1	0	0	0		
	750 ppm	0	0	0	0	0	1		
	1500 ppm	0	0	0	Ō	Õ	2		
	3000 ppm	0	0	Ő	Ő	Ő	Ō		
M.PERI MOUTH	Control	٥	٥	٥	0	0	0		
ALLERI MOOTH	750 ppm	0 1	0	0	0	0	0		
			1	1	1	1	1		
	1500 ppm	0	0	1	0	0	0		
	3000 ppm	0	0	0	0	0	0		
I.ORAL CAVITY	Control	0	1	1	1	1	1		
	750 ppm	0	0	0	0	0	0		
	1500 ppm	0	0	0	0	0	0		
	3000 ppm	0	0	0	0	0	0		
I.EAR	Control	0	0	0	0	0	0		
	750 ppm	1	1	1	1	1	1		
	1500 ppm	0	0	0	0	0	0		
	3000 ppm	0	0	0	0	0	0		
		v	v	v	v	v	v		
M.PERI EAR	Control	0	0	0	0	0	0		
	750 ppm	0	0	0	0	0	0		
	1500 ppm	0	0	0	0	0	0		
	3000 ppm	0	0	0	0	0	0		

STUDY NO. :	0267
ANIMAL :	RAT F344/DuCrj
REPORT TYPE	: A1 104

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : MALE

Clinical sign	Group Name	Admini	stration We	eek-dav											
		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	14-7
NECH		_													
I.NECK	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
FORLIMB	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1.BREAST	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	. 0	0	0	Ő	0	õ	õ
	1500 ppm	0	0	0	0	0	0	0	0	Ō	õ	Ő	Ő	Ő	ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	õ	Ő	Ő	õ
1. ABDOMEN	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Õ	õ
	1500 ppm	0	0	0	0	0	0	0	Õ	Õ	õ	õ	õ	õ	0
	3000 ppm	0	0	0	0	0	0	0	0	0	õ	õ	õ	õ	Õ
1.ANTERIOR.DORSUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	õ	õ	Ő
	1500 ppm	0	0	0	0	0	0	0	ò	Ō	õ	õ	õ	õ	õ
	3000 ppm	0	0	0	0	0	0	0	0	Ő	Õ	0	0	Õ	õ
1.POSTERIOR DORSUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	Ō	0	Ő	Ő	0	Õ	Õ	0
	1500 ppm	0	0	0	0	0	0	0	Õ	õ	õ	0	Õ	õ	0
	3000 ppm	0	0	0	0	Õ	0	Ő	õ	õ	Ő	0	0	0	0
4.HINDLIMB	Contral	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	Ö	Ő	Õ	Õ	Õ	õ	Ő	0	0	0	0	0	0
	1500 ppm	0	Ō	õ	Ő	õ	Ő	õ	ő	0	0	0	0	0	0
	3000 ppm	0	õ	Ő	õ	õ	Õ	0	õ	0 0	0	0	0	0	0
1.GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	õ	Õ	õ	Ő	Õ	õ	Ő	Ő	Ő	0	0	0	0	0
	1500 ppm	ŏ	õ	õ	õ	0	0	0	0	0	0	0	0	0	-
	3000 ppm	õ	0	0	õ	0	0	0	0	0	0	0	0	0	0 0

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M.NECK	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M.FORLIMB	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0.	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M.BREAST	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Ó	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Õ	0
M. ABDOMEN	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	Ō	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M.ANTERIOR.DORSUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M.POSTERIOR DORSUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M.HINDLIMB	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ő
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Õ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M.GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ő

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

18-7

19-7

20-7

21--7

22-7

23-7

24-7

25-7

26-7

27-7

17-7

Administration Week-day \_

16-7

15-7

Group Name

SEX : MALE

Clinical sign

(HAN190)

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS SEX : MALE

PAGE : 27

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Clinical sign	Group Name	Admin	stration W	eek-day											
	·	29-7	30-7	31-7	32-7	33-7	34-7	35-7	36-7	37-7	38-7	39-7	407	41-7	42-7
NECK		•		•				_	_						
.NECK	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
FORLIMB	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	· 0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
BREAST	Control	0	0	0	. 0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	o`
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M. ABDOMEN	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
.ANTERIOR, DORSUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ó	Ō
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
.POSTERIOR DORSUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
HINDLIMB	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	Ō	Õ	ŏ	ů
	1500 ppm	0	0	0	0	Ō	0	0	Ő	õ	ů	õ	Ő	õ	Ő
	3000 ppm	0	0	0	0	0	0	0	Ő	õ	Ő	Õ	Ő	Ő	õ
I.GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	Ō	Ō	Ō	Õ	õ	Õ	Ő	ŏ	0
	1500 ppm	Ō	0	0	0	0	Ő	Ō	õ	õ	Õ	õ	Ő	Ő	õ
	3000 ppm	0	0	0	0	Ō	Ō	Ō	0	ŏ	Ő	õ	0 0	Ő	0 0

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day													
		43-7	44-7	457	46-7	47-7	48-7	49-7	50-7	51-7	52-7	53-7	54-7	55-7	56-7
NECK	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Ó	0	õ
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	. 0	0	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	Ő	ő	0	õ
FORLIMB	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ō	Ő
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	Õ	Ő	Ő
	3000 ppm	0	0	0	0	0	0	0	Ő	0	õ	õ	õ	Ő	õ
1.BREAST	Centrol	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	Ō	0	Ō	Õ	õ	Ő	õ	Ő	ŏ	Ő	0	0
	1500 ppm	Ō	Õ	Õ	õ	õ	õ	ů	ŏ	Ő	0	ŏ	ŏ	0	0
	3000 ppm	0	0	0	0	Ő	Ő	0	õ	õ	Ő	õ	Õ	0	0
N. ABDOMEN	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	Ō	Ō	0	Ő	Ő	õ	0 0	Ő
	1500 ppm	0	0	0	0	Ő	Ő	õ	Ő	Ő	Ő	Ő	ŏ	0	0
	3000 ppm	0	0	0	0	0	Ô	Õ	. 0	Ő	ő	Ő	0	0	0
A.ANTERIOR, DORSUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	Ō	Ó	0	Ő	Ő	Õ	õ
	1500 ppm	0	0	0	0	0	0	0	Ó	0	Õ	õ	Õ	õ	õ
	3000 ppm	0	0	0	0	0	0	0	0	Ő	Ő	Ő	õ	Ő	0
POSTERIOR DORSUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	Ó	Ō	Õ	Õ	Õ	õ	Õ	0 0	Ő	Ő	0	0
	1500 ppm	0	0	0	Ő	0	Ō	õ	Ő	Ő	Ő	Õ	Ő	0	
	3000 ppm	0	õ	Ő	õ	ő	Ő	Õ	0	õ	0	0 0	1	1	0 1
M.HINDLIMB	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	Ō	Õ	0	õ	õ	Ő	Ő	0	õ	0	0	0
	1500 ppm	õ	0	õ	õ	0	0	õ	0	õ	0	0	0	0	0
	3000 ppm	õ	Ő	Ő	õ	ő	õ	ŏ	0	0	0	ŏ	0	0	0
M.GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ō	Ő	Ő	õ	Ő	Ő	ů 0	Ő	0	Ő	õ	Ő	0	0
	1500 ppm	Ő	Õ	Ő	Ő	õ	Õ	õ	õ	õ	0	0	0	0	0
	3000 ppm	Õ	õ	ů	Ő	õ	õ	0	ŏ	õ	0	0	0	0	. 0

STUDY NO. :	0267
ANIMAL :	RAT F344/DuCrj
REPORT TYPE	: A1 104

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : MALE

linical sign	Group Name	Admini	stration W	eek-day											
	·	57-7	58-7	59-7	60-7	61-7	62-7	63-7	64-7	65-7	66-7	67-7	68-7	69-7	70-7
NECK	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
FORLIMB	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
BREAST	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	Ó	0	Ō	0	0	0 0	Ő	Õ	Ő
	1500 ppm	0	0	0	0	0	0	1	1	1	1	1	1	Õ	Ő
	3000 ppm	0	0	0	0	0	Ō	ō	Ō	ō	ō	ō	0	õ	ŏ
1. ABDOMEN	Control	0	0	0	0	0	0	0	0	1	1	1	1	1	1
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Ō	Ō	õ
	1500 ppm	0	0	0	0	0	0	0	0	Ō	0	0	Ő	Ō	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	Ő	õ	õ	õ
ANTERIOR, DORSUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ó	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
POSTERIOR DORSUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Ō	0	Ō	Ő
	3000 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
.HINDLIMB	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	Ō	0	0	0	Ő	õ	Ő	ů	Ő	Ő	õ
	1500 ppm	0	0	Ō	0	Ō	õ	0	õ	ů	Ő	ů	0	0	0
	3000 ppm	0	Ő	õ	Ő	Õ	Ő	Ő	õ	õ	õ	õ	0	0	0
GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Õ	Õ	Ő	ŏ	Ő	Ő	ŏ	Ő	0 0	õ	õ	õ	Õ	0
	1500 ppm	õ	Õ	Õ	õ	õ	õ	õ	0	0 0	Ő	0	0	0	0
	3000 ppm	Ő	õ	õ	õ	0	1	1	õ	0	0	0	0	0	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\sim$ 

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SEX : MALE

Clinical sign	Group Name	Admin	istration W	leek-day														
		71-7	72-7	73-7	747	75–7	76-7	77–7	787	79–7	807	81-7	82-7	83-7	84-7			
I. NECK	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
	750 ppm	0	0	0	0	0	0	0	0	0	0	Ó	0	0	0			
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Ō	0	0	Ő			
	3000 ppm	0	0	0	0	0	0	0	0	0	0	Ő	õ	õ	0			
FORLIMB	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	õ	Õ			
I.BREAST	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	. 0			
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Ő	Õ	Ő	Ő			
	3000 ppm	0	0	0	0	0	0	0	Ō	Ő	0	Ő	õ	õ	Ő			
M. ABDOMEN	Control	1	1	1	1	1	1	1	1	1	1	1	1	1	1			
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ő			
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	1	0	0			
.ANTERIOR.DORSUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	1	1	1			
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
POSTERIOR DORSUM	Control	1	1	1	1	0	1	1	1	1	0	0	0	0	0			
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ő			
	3000 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1			
L.HINDLIMB	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
	1500 ppm	0	0	0	0	0	0	0	0	0	0	õ	õ	0	0			
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
I.GENITALIA	Control	0	0	0	0	0	0	0	1	1	1	1	1	1	2			
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
	1500 ppm	0	0	0	0	0	0	. 0	0	0	0	0	0	0	0			
	3000 ppm	0	0	0	0	0	0	0	0	0	1	1	1	1	1			

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\sim$ 

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SEX : MALE

		85-7	stration W												
			86-7	87-7	88-7	89-7	90-7	917	92-7	93-7	94–7	95-7	96–7	97–7	98-7
I.NECK	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	1	1	1	1	1	1	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	1	1	1
FORLIMB	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
I. BREAST	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	Ō	0	Ő	õ	õ	0	1	1	1
	1500 ppm	0	Ō	Õ	Ō	õ	Ő	õ	õ	õ	Ő	Õ	0	0	0
	3000 ppm	Ő	Ő	õ	ő	Õ	õ	õ	0 0	õ	õ	0 0	0	0	õ
1. ABDOMEN	Control	1	1	1	1	1	1	1	1	I	1	3	3	3	3
	750 ppm	0	0	0	0	1	1	1	1	1	2	2	2	2	2
	1500 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	3000 ppm	õ	ō	ō	ō	Ō	Ō	ò	ō	Ō	ō	0	0	. 0	0
I.ANTERIOR.DORSUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	1	1	1	1	1	1	1	1	1	1	1	2	2	2
	1500 ppm	0	0	0	0	Ō	Ō	ō	ō	0	ō	ō	õ	õ	Õ
	3000 ppm	0	0	0	0	0	0	0	Ő	Ő	1	ı 1	1	1	1
POSTERIOR DORSUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	1	1	1	1	1	1
	1500 ppm	1	1	ĩ	1	1	1	1	1	1	1	1	1	1	1
	3000 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1.HINDLIMB	Contral	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	Õ	Ő	õ	0	ŏ	õ	Ö	õ	1	1	1	1	1
	1500 ppm	Ő	õ	õ	0	0	Ő	0	0	0	0	0	0	0	1 0
	3000 ppm	Ő	0	Ö	õ	0 0	0	0	0	ŏ	0	0	0	0	0
I.GENITALIA	Control	2	3	3	2	2	2	2	2	2	2	0	0	ó	0
	750 ppm	0	0	0	0	0	Ő	0 0	0	0	0	0	0	0	0
	1500 ppm	ŏ	0	0	0	0 0	0	0	0	0	0	0	0	0	
											1				0 1
	3000 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : MALE

Clinical sign Group Name Administration Week-day 99-7 100-7 101-7 102-7 103-7 104-7 M.NECK Control 750 ppm 1500 ppm 3000 ppm M.FORLIMB Control 750 ppm 1500 ppm 3000 ppm M.BREAST Control 750 ppm 1500 ppm 3000 ppm M. ABDOMEN Control 750 ppm 1500 ppm 3000 ppm M.ANTERIOR.DORSUM Control 750 ppm 1500 ppm 3000 ppm M.POSTERIOR DORSUM Control 750 ppm 1500 ppm 3000 ppm M.HINDLIMB Contral 750 ppm 1500 ppm 3000 ppm M.GENITALIA Control 750 ppm 1500 ppm 3000 ppm 

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\smile$ 

SEX : MALE

Clinical sign	Group Name	Admini	stration We	ek-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	14-7
.TAIL	Contral	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
NEMIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
RUSTA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	Ō	0	0	ō	Ő	Ő	õ
	1500 ppm	0	0	0	0	Ó	0	Ō	Ō	Ō	ō	Ō	Õ	Ő	ŏ
	3000 ppm	0	0	0	0	0	Õ	Ő	Õ	õ	Õ	õ	0	0 0	õ
RREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	õ	Õ	0	Õ	Ő
	1500 ppm	0	0	0	0	0	Ő	Õ	Õ	õ	Õ	Õ	õ	0.	0
	3000 ppm	0	Ō	õ	Ő	Õ	õ	õ	õ	õ	õ	õ	0	0	õ
ESPIRATORY SOUND ABNOR	Control	0	0	0	0	0	0	0	0	0	0	. 0	0	0	0
	750 ppm	0	0	0	Ō	Ő	Ő	Õ	õ	õ	Ő	õ	Ő	õ	0
	1500 ppm	Ō	0	Ō	Õ	Ő	Ő	Ő	õ	Ő	õ	Ő	Ő	õ	õ
	3000 ppm	0	0	0	Õ	0 -	Ő	Õ	Ő	Ő	Ő	Ő	õ	0	0
IOISY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ő	Õ	õ	õ	0 0	0	õ	0	Ő	0	0	0	0	0
	1500 ppm	õ	Ő	0	ŏ	0	Ő	0	0	0	0	0	0		-
	3000 ppm	ŏ	0	. 0	õ	0	0	0	0	0	0	0	0	0 0	0 0
ABNORMAL RESPIRATION	Contral	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	Õ	0	0	0	0	0	0	0	0	0	0		
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	•	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0 0	0 0	0 0
BNORMAL RESPIRA.SOUND	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Browning RED INA. OUND	750 ppm	0	0	0	ő	0	0	0	0	0	0	0	0		0
	1500 ppm	0	0	0	0	0	0	0	0	0	•	•	•	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		v	v	U	v	v	v	v	v	v	U	0	0	0	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\sim$ 

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## SEX : MALE

PAGE: 34

Clinical sign	Group Name	Admini	stration W	leek-day											
	·	15–7	167	17-7	18–7	19-7	20-7	21-7	22-7	23-7	24-7	25-7	26-7	27-7	28-7
										•••••••					
TAIL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
NEMIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	Õ	0	Õ	0	0
	3000 ppm	0	0	0	0	0	0	ō	õ	õ	Ő	0	õ	0 0	0
CRUSTA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Õ	Ő	õ
	1500 ppm	0	0	0	0	0	0	0	Ō	0	Ō	Ő	Õ	Ő	0 0
	3000 ppm	0	0	0	0	0	0	0	õ	õ	Ő	Ő	ő	0	0
RREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0.0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ő
	1500 ppm	0	0	0	0	0	0	0	Ō	0	Õ	Ő	Ő	Õ	0
	3000 ppm	0	0	0	0	0	0	0	0	õ	0	õ	0	0 0	õ
RESPIRATORY SOUND ABNOR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	Ó	Ō	Ō	õ	Õ	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	õ	õ	0	0
NOISY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	Ő	õ	Ő	Õ	Ő	Ő	Ô
	1500 ppm	0	0	0	0	0	0	Ő	0	õ	Ő	Ő	Ő	Ő	Ő
	3000 ppm	0	0	0	Ō	0	õ	õ	0	Ő	õ	õ	0	0	0
ABNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	Ō	Ō	õ	Ő	õ	õ	0	õ	0	0	0
	1500 ppm	0	0	Õ	õ	õ	õ	Ő	õ	õ	0 0	0	0	0	0
	3000 ppm	0	0	0	Ō	, Ŏ	Ő	õ	õ	0	0	õ	0	0	0
ABNORMAL RESPIRA.SOUND	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	Ó	Ō	Ō	Õ	õ	Õ	0	0	0
	1500 ppm	0	0	0	0	0	Ō	Ő	õ	Õ	Ő	Ő	Ő	0	ŏ
	3000 ppm	0	0	0	0	Ö	0	Õ	0	Õ	õ	0	0 0	0	ŏ

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : MALE

Clinical sign	Group Name	Admin	istration W	leek-day											
	Al	29-7	307	31-7	32-7	33-7	34-7	35-7	36-7	37-7	38-7	39-7	40-7	41-7	42-7
							1. 111.1								
.TAIL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ō
	1500 ppm	0	0	0	0	0	0	0	0	0	0	. 0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Õ	Ő
VEMIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Õ	0
	3000 ppm	0	0	0	0	0	0	0	0	0	õ	õ	õ	õ	ů 0
RUSTA	Control	0	0	0	0	0	0	0	0	0	· 0	0	0	0	
	750 ppm	0	Ō	0	Ō	Ő	õ	õ	Ő	Ő	õ	õ	0	0	0
	1500 ppm	ō	õ	Õ	Ŏ	õ	Ö	ŏ	ŏ	õ	0	0	0	0	0
	3000 ppm	Õ	õ	õ	õ	õ	0 0	õ	0	0	0	0	0	0	0
RREGULAR BREATHING	Contral	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	Ó	0	0	Ő	Õ	õ	õ	Õ	õ	õ	0	0	0
	1500 ppm	0	Ō	õ	Ő	õ	õ	õ	ŏ	õ	õ	0	0	ŏ	0
	3000 ppm	0	õ	õ	õ	Ő	0	õ	0	0	0	0	0	0	0
ESPIRATORY SOUND ABNOR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	Ő	Õ	Õ	Õ	Ő	õ	õ	õ	Ő	0	0	0
	1500 ppm	Ó	Ó	Ō	0	Õ	Õ	õ	Ő	õ	õ	Õ	Ő	õ	0
	3000 ppm	0	0	0	Ō	õ	õ	õ	ő	õ	õ	õ	õ	õ	0
OISY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	Ó	0	Ō	0	0	õ	õ	õ
	1500 ppm	0	0	Ő	Ő	Õ	Õ	õ	õ	õ	0	0	õ	õ	0
	3000 ppm	Ő	Ő	õ	0	Ő	õ	õ	õ	0 0	0 0	0	0	0	0
BNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ő	õ	Õ	õ	Õ	õ	õ	Ő	0	0	0	0	0	0
	1500 ppm	Ő	ŏ	0 0	Ö	0	0	0	0	0	0	0	0	0	0
	3000 ppm	Ő	õ	0	Ő	õ	0	0	0	0	0	0	0	0	0
BNORMAL RESPIRA.SOUND	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ő	Ő	Ő	0	Ö	0	0	0	0	0	0	0	0	. 0
	1500 ppm	õ	õ	ŏ	0	Ő	0	0	0	0	0	0	0	-	
	3000 ppm	0	0	0	Ő	0	0	0	0	0	0	0		0	0
		v	v	v	v	v	v	v	v	v	v	v	0	0	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : MALE

Clinical sign	Group Name	Admini	stration W	eek-day											
		43-7	44-7	45-7	46-7	47-7	48-7	49-7	50-7	51-7	52-7	53-7	54-7	55-7	56-7
											•				
.TAIL	Control	0	0	0	0	0	0	0	0	0	1	1	1	1	1
	750 ppm	0	0	0	0	0	0	0	0	0	. 0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	1	1	1	1	1
	3000 ppm	0	0	0	0	0	0	0	0	0	ō	0	ō	Ô	Ō
NEMIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	Ō	0	0	Ő	Ő	Ő
	3000 ppm	0	0	0	0	0	0	0	õ	Ő	õ	Ő	õ	0	õ
CRUSTA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Ō	Õ	õ
	1500 ppm	0	0	0	0	0	0	0	0	0	0.	Ó	0	0	Õ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ő	Õ
RREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	Ő	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
RESPIRATORY SOUND ABNOR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
NOISY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Ō	Ō	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	õ	õ	õ	ŏ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0 0	Ő	õ
ABNORMAL RESPIRA.SOUND	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	Ō	õ	Ő	Ő
	1500 ppm	0	0	0	0	0	0	0	0	Ō	0	Ő	õ	Ő	õ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	Ő	õ	õ	Õ

STUDY NO. :	0267
ANIMAL :	RAT F344/DuCrj
REPORT TYPE	: A1 104

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : MALE

Clinical sign	Group Name	Admini	stration W	eek-day											
		57-7	58-7	59-7	60-7	617	62-7	63-7	64-7	65-7	66-7	67-7	68-7	69-7	70-7
.TAIL	Contral	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	3000 ppm	0	0	0	0	0	0 -	0	0	0	0	0	0	0	0
NEMIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 maa	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CRUSTA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ō	0
	1500 ppm	0	0	0	0	0	0	0	Ó	Ō	Õ	Õ	Õ	Õ	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	Ō	õ	õ	Ő
RREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ō
	1500 ppm	0	0	0	0	0	0	Ó	Ō	0	0	0	0	Ő	õ
	3000 ppm	0	0	0	0	0	0	Ő	Ő	õ	Ő	õ	0	0	Ő
ESPIRATORY SOUND ABNOR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	Ő	Õ	õ	Õ	Õ	Ő
	1500 ppm	0	0	0	0	Ō	Ō	0	õ	ŏ	Ő	ů	õ	Õ	0
	3000 ppm	0	0	0	0	Ő	0	Ő	Ő	õ	õ	õ	0	0	0
IOISY	Contral	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ō	0	0	õ	Õ	õ	õ	Ő	Ő	0	0	Ő	Ő	Ő
	1500 ppm	Õ	0	Õ	õ	ő	õ	ŏ	õ	ŏ	0	0	õ	0	0
	3000 ppm	õ	Ő	õ	õ	Ő	õ	õ	õ	Ő	0	0 0	0	0	0
BNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ő	0	Õ	Ő	Ő	Ő	õ	Õ	0	0 0	0	0	0	0
	1500 ppm	õ	0 0	õ	õ	Ő	Ő	ŏ	õ	0	0	ŏ	0	0	0
	3000 ppm	Ő	Ő	0	Ő	Ő	õ	õ	õ	õ	ŏ	õ	0	0	0
BNORMAL RESPIRA.SOUND	Contral	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	õ	õ	Ő	ŏ	Ő	õ	ů 0	ŏ	Ő	Ő	0	0	0	0
	1500 ppm	Ő	õ	Ő	ů 0	0	0	õ	0	0	0	0	0	0	-
	3000 ppm	Ö	õ	ŏ	0	0	0	Ő	0	0	0	0	0	0	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\dot{\phantom{a}}$ 

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SEX : MALE

Clinical sign	Group Name	Admin	istration W	eek-dav											
		71-7	72-7	73-7	74-7	75-7	76-7	77-7	78-7	79-7	80-7	81-7	82-7	83-7	84-7
				- m n			·						· · · · · · · · · · · · · · · · · · ·		
1.TAIL	Control	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	750 ppm	0	0	0	0	0	0	0	0 .	0	0	0	0	0	2
	1500 ppm	1	1	1	1	0	0	0	1	1	1	1	1	1	1
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
NEMIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Ó	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	Õ ·	õ	Ő
RUSTA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Ō	0	0	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ő
RREGULAR BREATHING	Control	0	0	0	1	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ESPIRATORY SOUND ABNOR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
IOISY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	1	1	1	0	0
BNORMAL RESPIRATION	Control	0	0	0	1	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	Ō	0	0
BNORMAL RESPIRA.SOUND	Contral	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ō
	3000 ppm	0	0	0	0	0	0	0	0	0	1	1	1	0	Ő

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS -

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SEX : MALE

Clinical sign	Group Name	Admin	istration W	eek-day							•			•••••••	
		85-7	86-7	87-7	88-7	89-7	90-7	91-7	92-7	93-7	94-7	95-7	96-7	97-7	98-7
													<u></u>		
.TAIL	Contral	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	750 ppm	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	1500 ppm	0	0	0	0	0	0	0	0	0	ō	. õ	õ	õ	õ
	3000 ppm	0	0	0	0	0	0	0	0	0	Õ	õ	Ő	õ	1
NEMIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Õ	Ő	õ
	1500 ppm	0	0	0	0	0	0	0	Ő	õ	õ	0	Ő	Ő	Ő
	3000 ppm	0	0	0	0	0	Ō	0	Ő	0 0	õ	0	0	0	0
RUSTA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	õ	õ	Ő	Ő	0
	1500 ppm	0	0	0	0	Ō	Õ	Õ	õ	õ	ŏ	0	0 0	1	1
	3000 ppm	0	0	0	0	õ	Õ	Õ	õ	Ő	0	0	0	0	0
RREGULAR BREATHING	Control	0	0	0	0	1	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	ō	Ō	0	õ	ŏ	Õ	0	0	0	-
	1500 ppm	0	0	Ō	õ	õ	õ	Õ	ŏ	0	0	ŏ	0	1	0
	3000 ppm	0	0	0	õ	õ	õ	õ	õ	0	0	0	0	1	0 0
ESPIRATORY SOUND ABNOR	Control	0	1	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	Ō	Ō	õ	õ	Ő	0	Ő	0	0	0	0
	1500 ppm	0	ō	Ő	ŏ	Ő	Õ	ŏ	Ő	Ő	0	0	0		-
	3000 ppm	0	Ö	0	Ő	ő	0	0	0	0	0	0	0	0 0	0 0
OISY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	õ	õ	õ	Õ	. 0	Ő	0	0	0	0	0
	1500 ppm	õ	Ő	õ	Õ	õ	ŏ	0	0	0	0	0	0	0	0
	3000 ppm	õ	0	õ	Õ	õ	ŏ	0	0	0	0	0	0	0 0	0 0
BNORMAL RESPIRATION	Control	0	0	0	0	1	0	0	0	0	0	0	0	^	^
	750 ppm	0	õ	0 0	Ő	Ō	Ö	0	0	0	0	-	-	0	0
	1500 ppm	õ	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	õ	ő	õ	0 0	ŏ	0	0	0	0	0	0 0	0	1 0	0
BNORMAL RESPIRA.SOUND	Control	0	1	0	0	0	0	0	0	0	0		1		
· · · · · · · · · · · · · · · · · · ·	750 ppm	õ	ō	Ő	0	0	0	0	0	•	•	1	1	1	1
	1500 ppm	0	0	0	0	0	0	0		0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0		0	0	0	0	0	0	0
		v	v	v	v	U	U	0	0	0	0	0	0	0	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\sim$ 

#### SEX : MALE

Clinical sign Group Name Administration Week-day 99-7 100-7 101-7 102-7 103-7 104-7 M.TAIL Control 750 ppm 1500 ppm 3000 ppm ANEMIA Control 750 ppm 1500 ppm 3000 ppm CRUSTA Control 750 ppm 1500 ppm 3000 ppm IRREGULAR BREATHING Control 750 ppm 1500 ppm 3000 ppm RESPIRATORY SOUND ABNOR Control 750 ppm 1500 ppm 3000 ppm NOISY Control 750 ppm 1500 ppm 3000 ppm ABNORMAL RESPIRATION Control 750 ppm 1500 ppm 3000 ppm ABNORMAL RESPIRA. SOUND Control 750 ppm 1500 ppm 3000 ppm 

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : MALE

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Clinical sign	Group Name	Admini	stration We	əek-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	14-7
		_													
IEMATURIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
YELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Õ	õ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
OLIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	. 0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	õ	Ő	Ő
	3000 ppm	0	0	0	0	Ō	0	Ō	0	õ	0	õ	Ő	õ	0 0

(HAN190)

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : MALE

PAGE: 42

Clinical sign	Group Name	Admini	istration W	eek-day _											
		15–7	16-7	17-7	18-7	197	20-7	21-7	22-7	23-7	24-7	25-7	26-7	27-7	28-7
IEMATURIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	. 0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
OLIGO-STOOL	Control	0	0	0	0	0	0	0	. 0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

(HAN190)

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : MALE

Clinical sign	Group Name	Admini	stration W	eek-day											
		29-7	30-7	31-7	32-7	33-7	347	35-7	36-7	37-7	38-7	39-7	40-7	41-7	42-7
													***		
HEMATURIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ō
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	Ō	Ő	Ő
OLIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Õ	õ
	3000 ppm	0	0	0	0	0	0	0	0	õ	0	õ	õ	0	õ

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(HAN190)

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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REPORT TYPE : A1 104 SEX : MALE 

Clinical sign	Group Name	Admini	stration W	leek-day											
		43-7	44-7	45-7	46-7	477	48-7	49-7	50-7	51-7	52-7	53-7	54-7	55-7	56-7
HEMATURIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
YELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
OLIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	Ō	Ō	Ō	Ō

(HAN190)

Clinical sign	Group Name	Admini	stration V	leek−day											
	·	57-7	58-7	59-7	60-7	61-7	627	63-7	64-7	65-7	66-7	67–7	68-7	69-7	70-7
IENATURIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	Ō	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
YELLOW URINE	Contral	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	. 0	0
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DLIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

(HAN190)

STUDY NO. : 0267

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

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## CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : MALE

Clinical sign	Group Name	Admini	stration W	eek~day											
<u></u>	······································	71-7	727	73–7	74–7	75-7	76-7	77–7	78–7	797	807	81-7	82-7	83-7	84-7
													_	_	
HEMATURIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
YELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	. 0	0	0	0	0
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	2	0	0
OLIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	1	0	Ó

(HAN190)

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

REPORT TYPE : A1 10 SEX : MALE

PAGE: 47

Clinical sign	Group Name	Admini	istration W	eek-day											
		85-7	86-7	87–7	88-7	89-7	90-7	91-7	92-7	937	94-7	95-7	96-7	97-7	98-7
												,			
HEMATURIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	1	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SHALL STOOL	Control	0	0	1	1	1	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
OLIGO-STOOL	Control	1	2	2	2	2	1	1	1	1	2	0	0	0	1
	750 ppm	1	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	1	0	0	0	0	0	1	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ő	0

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : MALE

PAGE : 48

Clinical sign	Group Name	Admin	istration	leek-day			
		99-7	100-7	101-7	102-7	103-7	104-7
*** *********************************							
HEMATURIA	Control	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0
	3000 ppm	0	0	0	0	1	1
YELLOW URINE	Control	1	1	0	0	1	0
	750 ppm	ō	Ô	Ő	Õ	Ô	0
	1500 ppm	Ő	Ő	Õ	Ő	Ő	õ
	3000 ppm	Ō	0	Ő	0	Õ	0
SMALL STOOL	Control	1	2	0	1	1	0
	750 ppm	1	1	0	0	0	0
	1500 ppm	0	0	0	0	0	0
	3000 ppm	0	0	1	1	0	0
OLIGO-STOOL	Control	1	2	0	1	1	0
	750 ppm	1	1	0	0	0	0
	1500 ppm	0	1	0	0	0	0
	3000 ppm	0	0	1	1	0	0

(HAN190)

APPENDIX A 2

# CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(2-YEAR STUDY)

STUDY NO. :	0267
ANIMAL :	RAT F344/DuCrj
REPORT TYPE	: Al 104

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\sim$ 

# SEX : FEMALE

PAGE: 49

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Clinical sign	Group Name	Adminis	stration We	ek-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	14-7
EATH	Control	•	0	0	0	0	0	٥	•	•	0		<u>^</u>	0	0
LAIN	Control 750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm 3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	-	0
	anna bhu	U	0	U	V	U	U	U	U	U	U	U	U	0	0
ORIBUND SACRIFICE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	õ	0	0	Ō	0
OCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	. 0
Soonoron novement prot	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	ann bhu	v	v	v	v	U	v	v	v	v	v	U	U	v	U
UNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PARALYTIC GAIT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	Ō	Ō	Ō	Ő	0	0	0	Ő	Ő	Ő
	1500 ppm	Ō	Ō	Õ	0	Ő	õ	õ	Õ	õ	Ő	0	õ	Ő	õ
	3000 ppm	õ	Ő	Ő	õ	ů	Ő	Õ	Ő	õ	Ő	0 0	0	0	õ
WASTING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SOILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	õ	0	Ő	Õ	Õ	Ő	Õ	õ	Ő	õ	Ô	0	Ô	Ő
	1500 ppm	õ	õ	õ	ů -	õ	õ	õ	õ	Ő	0	õ	0	0	0
	3000 ppm	Ő	Ô	0	0	0	0	0	0	0	0	. 0	0	0	0
		v	v	v	v	v	v	v	v	v	v	v	v	v	U
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : FEMALE

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

Clinical sign	Group Name	Admini	stration W	leek-day											
	····	15-7	16-7	17-7	18-7	19-7	207	21-7	227	23-7	24-7	25-7	26-7	27-7	28-7
РЕАТН	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
JEATH	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		0	0	0	0	0	0	0	0	0	-	0	0	0	-
	3000 ppm	U	U	U	U	U	U	0	v	U	0	U	U	0	0
ORIBUND SACRIFICE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
OCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	Ó	0	0	0	0	Ő	0	0
	1500 ppm	0	õ	Ő	Õ	Õ	Õ	Õ	Õ	Õ	0	Ő	Õ	Õ	0 0
	3000 ppm	Õ	Õ	Õ	Õ	õ	ŏ	Ō	Õ	Õ	Õ	Ő	Ő	õ	õ
UNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
UNCHDROR FUSIFIUM	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		•	0	0	-		•	-	-	-	•	•		•	-
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	U	U	0	0	0	0	0	0	0	0	0	0	0
ARALYTIC GAIT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ASTING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
OILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	õ	Õ	Ő	Ő	ŏ	Ő	Ő	Ő	õ	0 0	Ő	0	Ő	Ő
	1500 ppm	õ	Ő	Ő	ŏ	õ	õ	õ	ő	Ő	õ	0	0	õ	0 0
	3000 ppm	Ö	Ő	Ő	Ő	õ	Ő	õ	õ	0	Ö	0	0	0	0
		-	-		-	-		-	-	-	-	-	-	•	v
PILOERECTION	Control.	0	0	0	0	0	0	0	0.	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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Clinical sign	Group Name	Admini	stration W	eek-day _											
		29-7	307	31-7	327	33-7	34-7	35-7	36-7	37-7	38-7	39-7	40-7	41-7	42-7
DEATH	Control	0	0	0	0	٥	٥	٥	0	٥	0	0	٥	0	0
JEATH	Control 750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	v	V	V	V	U	v	V	U	U	U	U	v	U	U
ORIBUND SACRIFICE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	ŏ	õ	õ	Õ	õ	õ	Õ	õ	õ	Ő	Ő	Ő	0	õ
	1500 ppm	ŏ	õ	ŏ	õ	õ	ŏ	Ő	õ	õ	õ	Õ	õ	õ	õ
	3000 ppm	ŏ	Ő	õ	õ	õ	õ	õ	õ	0 0	õ	ő	0	ŏ	Õ
		v	v	v	v	v	v	v	v	v	Ū	v	v	v	v
OCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
UNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ő	õ	ŏ	0 0	Ő	õ	Õ	õ	ů.	õ	Ő	0	õ	0 0
	1500 ppm	0	Õ	ŏ	Ő	0 0	õ	Ő	õ	õ	ŏ	Ô	0	Ő	0 0
	3000 ppm	0	0	0	0	ŏ	Ő	0	0	0	0	0	0	0	0
		v	v	v	v	v	v	v	v	v	v	v	v	U	U
ARALYTIC GAIT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ó
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DASTING	Court and	0	0	0	0	0	0	0	0	0	0	0	0	0	
VASI ING	Control 750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			-	-						-	-	•	•	•	•
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
OILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	Ō	0	Ō	0	0	0	0	Ō	0	0	0	Ō	0	Ő
	3000 ppm	0	Ő	0	0	Ő	Ő	0	0	Ő	Ő	õ	Õ	Ő	Õ
H OCDCCTION	Control	0	0	٥	0	0	0	٨	0	0	0	^	0	^	0
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
	750 ppm	0	•	-		-	-	•		•	•	•	0	•	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

SEX : FEMALE

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104 CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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MORIBUND SACRIFICE	Control	0	0	0	0	0	0	0	0	0	
	750 ppm	0	0	0	0	0	0	0	0	0	
	1500 ppm	0	0	0	0	0	Ō	0	0	õ	
	3000 ppm	Ō	Ō	0	Ō	õ	õ	õ	õ	õ	
								-	·	•	
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	
	750 ppm	0	0	0	0	0	0	0	0	0	
	1500 ppm	0	0	0	0	0	0	0	0	0	
	3000 ppm	0	0	0	0	0	0	0	0	0	
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	
	750 ppm	0	0	0	0	0	0	0	0	0	
	1500 ppm	0	0	0	0	0	0	0	0	0	
	3000 ppm	0	0	0	0	0	0	0	0	0	
PARALYTIC GAIT	Control	0	0	0	0	0	0	0	0	0	
	750 ppm	0	0	0	0	0	0	0	0	0	
	1500 ppm	0	0	0	0	0	0	0	0	0	
	3000 ppm	0	0	0	0	0	0	0	0	0	
WASTING	Control	0	0	0	0	0	0	0	0	0	
	750 ppm	0	0	0	0	0	0	0	0	0	
	1500 ppm	0	0	0	0	0	0	0	0	0	
	3000 ppm	0	0	0	0	0	0	0	0	0	
SOILED	Control	0	0	0	0	0	0	0	0	0	
	750 ppm	0	0	0	0	0	0	0	0	0	
	1500 ppm	0	0	0	0	0	0	0	0	0	
	3000 ppm	0	0	0	0	0	0	0	0	0	
DIL OPDECTION	0	•	•	•	•	0	<u>,</u>				
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	
	750 ppm	0	0	0	0	0	0	0	0	0	
	1500 ppm	0	0	0	0	0	0	0	0	0	
	3000 ppm	0	0	0	0	0	0	0	0	0	

Group Name

Control

750 ppm

1500 ppm

3000 ppm

SEX : FEMALE

Clinical sign

DEATH

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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48-7

49-7

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45-7

Administration Week-day

44-7

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : FEMALE

Linical sign	Group Name	Admini	stration W	eek-dav											
		57-7	58-7	59-7	60-7	61-7	62-7	637	64-7	65-7	66-7	67-7	68-7	69-7	70-7
					_	_			_						
EATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DRIBUND SACRIFICE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
OCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
UNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ARALYTIC GAIT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ASTING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
OILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	õ	õ	0	0	Õ	Ō	0	0	0	0	0	0	0	0
	3000 ppm	Ő	Ő	0	Ō	Ō	0	0	Ő	Ō	0	0	0	Ő	Ō
ILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ő	0	Õ	Ō	0	0	Ō	0	0	Ō	0	0	0	0
	1500 ppm	õ	õ	õ	õ	Ő	Ō	Ő	Ő	Õ	Ō	Ō	0 0	Ő	Ő
	3000 ppm	õ	õ	õ	ĩ	ů	õ	õ	0	õ	Õ	Õ	0 0	Õ	Õ

STUDY NO. : 0267 ANIMAL : RAT F344/DJCrj REPORT TYPE : A1 104 SEX : FEMALE CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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Clinical sign	Group Name	Admini	stration W	eek-day											
		71-7	72-7	73-7	74-7	75-7	76-7	77-7	787	79-7	80-7	81-7	82-7	83-7	84-7
DEATH	Control	0	0	0	0	0	0	0.	0	0	0	0	0	0	0
Carn	750 ppm	õ	õ	õ	ŏ	õ	õ	0	õ	õ	õ	õ	õ	õ	õ
	1500 ppm	õ	Ő	Õ	Õ	Õ	Ő	Õ	õ	Õ	1	1	1	1	1
	3000 ppm	Ő	õ	Ő	1	1	2	2	2	2	2	3	3	3	4
ORIBUND SACRIFICE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	1	1	1	1	1
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	1	1	1	1	1	1	1	1	l	1
OCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	1	1	1	1	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	1	1	0	0	0	0	0	0	0	0	0
UNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	<i>,</i> 0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	1	0	0	0	0	0	0	0	0	0
PARALYTIC GAIT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
WASTING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	1	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	1	0	0	0	0	0	0	0	0	0
SOILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

# SEX : FEMALE

Clinical sign	Group Name	Admini	stration W	eek-dav											
		85-7	86-7	87-7	88-7	89-7	90-7	91-7	92-7	93-7	94-7	95-7	967	977	98-7
EATH	Control	0	0	0	0	0	0	. 0	1	2	3	3	5	5	5
	750 ppm	0	0	0	0	0	1	1	2	2	2	3	3	3	4
	1500 ppm	1	1	2	2	2	2	3	3	3	3	3	3	4	5
	3000 ppm	5	5	5	5	5	5	5	6	6	6	6	6	4 6	6
RIBUND SACRIFICE	Control	0	0	0	0	0	0	0	0	0	0	0	0	1	1
	750 ppm	2	2	2	2	2	2	2	2	2	2	2	2		
	1500 ppm	ō	ō	ō	õ	0	0	0	0	0	0			2	2
	3000 ppm	1	1	1	1	1 .	1	1	1	1	0 1	0 1	0 1	1 1	1 1
COMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	٥	^	0	0	•		_
	750 ppm	Ő	0	0	0	0	0	-	0	0	0	0	0	0	0
	1500 ppm	0	0	-			-	0	0	0	0	0	0	0	0
				0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
UNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	Ō
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	õ	0
RALYTIC GAIT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	Ō	0	õ	Õ	Ő
	1500 ppm	0	1	1	1	1	1	1	1	1	1	1	1	0 1	1
	3000 ppm	0	0	0	0	ō	ō	ō	Ō	ō	0	0	0	0	0
ASTING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	Ó	0	õ	õ	Ô	õ	Ő	0	0		
	1500 ppm	0	0	õ	õ	õ	Ő	0	0	0	0	•		0	1
	3000 ppm	Ő	Õ	Ő	õ	0	0	0	0	0	0	0 1	0 1	1 1	0 1
DILED	Control	0	0	0	0	0	0	0	0	0	0	٥	0	0	<u>^</u>
	750 ppm	Ő	Ő	0	0	0	0	0	0	0	•	0	0	0	0
	1500 ppm	õ	0	0	0	0	0		•	v	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		-	-	<u> </u>	•	v	v	v	v	v	v	U	0	0	0
ILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Ō	Õ	õ
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Ő	Ő	õ	Ö
	3000 ppm	0	0	0	0	0	0	0	0	0	Ō	Ő	Õ	0	Ő

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

#### SEX : FEMALE

Clinical sign Group Name Administration Week-day 99-7 100-7 101-7 102-7 103-7 104-7 DEATH Control 750 ppm 1500 ppm 3000 ppm MORIBUND SACRIFICE Control 750 ppm 1500 ppm 3000 ppm LOCOMOTOR MOVEMENT DECR Control 750 ppm 1500 ppm 3000 ppm HUNCHBACK POSITION Control 750 ppm 1500 ppm 3000 ppm PARALYTIC GAIT Control 750 ppm 1500 ppm 3000 ppm WASTING Control 750 ppm 1500 ppm 3000 ppm SOILED Control 750 ppm 1500 ppm 3000 ppm PILOERECTION Control 750 ppm 1500 ppm 3000 ppm 

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\sim$ 

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SEX : FEMALE

Clinical sign	Group Name	Admini	stration We	eek-dav					·· ····-			· · · · · · · · ·			
		1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	97	10-7	11-7	12-7	13-7	14-7
LOSS OF HAIR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	Ō	0	Õ	õ	õ	õ	õ	õ
	1500 ppm	0	0	0	0	0	0	0	Ō	Ō	Ő	Õ	Õ	ů	õ
	3000 ppm	0	0	0	0	0	0	0	0	0	Õ	õ	Õ	õ	Õ
OILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Ő	õ	ŏ
	1500 ppm	0	0	0	0	0	0	Ō	Õ	Ő	ŏ	Õ	0	0	Ő
	3000 ppm	. 0	0	0	0	0	Ő	Õ	õ	Ő	Ő	õ	0	Õ	Ő
EXOPHTHALMOS	Control	0	0	0	0	0	0	0	0	0	0	0	0	. 0	0
	750 ppm	0	0	0	0	0	0	Ō	õ	Ő	õ	õ	õ	0	0
	1500 ppm	0	0	0	0	0	0	0	Ő	Õ	õ	Ő	Ô	Õ	0
	3000 ppm	0	0	0	0	Ő	Ő	Õ	õ	Ő	ŏ	0 0	õ	0	0
EYE HEMORRHAGIC DISCHA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	Ō	Ō	Õ	õ	Ő	õ	ů 0	0
	1500 ppm	0	0	0	0	0	0	Ō	Ō	õ	0 0	0	0 0	õ	0
	3000 ppm	0	0	0	0	0	0	0	0	õ	Õ	0	õ	õ	õ
EYE OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	Ō	0	Ō	Õ	Ő	õ	ů 0
	1500 ppm	0	0	0	0	0	0	Ó	Ō	Ō	õ	Õ	Ő	õ	Õ
	3000 maa	0	0	0	0	0	0	0	0	0	õ	Ő	Õ	õ	õ
CATARACT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	Ō	0	0	ů	õ	õ
	1500 ppm	0	0	0	0	0	0	0	Ó	Ō	0	Õ	Ő	õ	ů 0
	3000 ppm	0	0	0	0	0	0	0	0	Õ	õ	õ	Õ	Õ	õ
CORNEAL OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	Õ	Ő	õ	Ő	. 0	õ
	1500 ppm	0	0	0	0	0	0	0	0	0	0	õ	õ	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	Ő	Ő	Ö	õ
EXTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Ō	õ	õ
	1500 ppm	0	0	0	. 0	0	0	0	0	0	0	0	0	Ő	õ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	õ

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\smile$ 

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SEX : FEMALE

Clinical sign	Group Name		stration W												
		15-7	16-7	17-7	18-7	19-7	20-7	21-7	22-7	23-7	24-7	25-7	26-7	27-7	28-7
												<u>,</u>			
OSS OF HAIR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	Ó	0	ō	Ő
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	õ	õ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ő	Õ
OILED PERI GENITALIA	Contral	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Ő	õ	õ
	1500 ppm	0	0	0	0	0	0	Ō	0	Õ	õ	õ	Ő	Ő	0
	3000 ppm	0	0	0	0	0	0	0	Ö	õ	õ	0 0	0	õ	0 0
EXOPHTHALMOS	Control	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	750 ppm	0	ō	ō	Ō	ō	ō	Ô	Ô	0	0	0	0	0	0
	1500 ppm	õ	Ő	ŏ	õ	0	Ő	0	0	0	0	0	0	0	
	3000 ppm	õ	õ	õ	ő	0	0	0	õ	0	0	0	0	0	0
EYE HEMORRHAGIC DISCHA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	Ō	0	Õ	ů 0	ů	0 0	0	Ő	0	0	0 0
	1500 ppm	0	Ō	Ő	õ	Õ	0	õ	Õ	0	0	0	0	0	0
	3000 ppm	0	0	Ō	õ	ő	0 0	õ	õ	o	0	0	0	0	0
EYE OPACITY	Control	0	0	0	0	1	0	1	1	1	1	1	۴	1	1
	750 ppm	0	0	0	0	0	0	0	0	ō	ō	0	Ō	Ô	.0
	1500 ppm	0	0	0	0	0	Ō	Ō	Ő	õ	Õ	Ő	õ	0	Ő
	3000 ppm	0	0	0	0	0	0	0	Ō	õ	Õ	0	0	0	0
CATARACT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	Ō	Õ	0	õ	õ	Ő	0	õ	0	0	0	0
	1500 ppm	0	0	0	Ő	0	Ő	õ	õ	õ	0	0	0	0	0
	3000 ppm	0	0	0	õ	õ	õ	õ	õ	0	0	0	0	0	0
CORNEAL OPACITY	Control	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	750 ppm	0	0	0	0	ō	Ō	õ	Ō	0	0	0	0	0	0
	1500 ppm	Ō	õ	õ	õ	õ	0	0	0	0	0	0	0	0	
	3000 ppm	0	Õ	Õ	õ	õ	0	0	õ	0	0	0	0	0	0
EXTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	.0
	750 ppm	Õ	õ	õ	Ő	Ő	Ö	0	0	0	0	0	0	0	
	1500 ppm	õ	ů 0	õ	0	0 0	0	0	0	0	ŏ	0	0		0
	3000 ppm	0	Ő	õ	Ő	Ő	0	0	0	0	0	0	0	0	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\sim$ 

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SEX : FEMALE

Clinical sign	Group Name	Admini	istration W	eek-dav											
	• • • • • • • • • • • • • • • • • • •	29-7	30-7	31-7	32-7	33-7	34-7	35-7	36-7	37-7	38-7	39-7	40-7	41-7	42-7
OSS OF HAIR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
OILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EXOPHTHALMOS	Control	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	750 ppm	0	0	0	0	0	0	0	0	0	0	ō	ō	0	0
	1500 ppm	0	0	0	0	0	0	0	Ō	0	Ő	Ő	Ő	Õ	0
	3000 ppm	0	0	0	0	0	0	0	0	0	Ő	Ő	õ	Ő	Ő
EYE HEMORRHAGIC DISCHA	Control	0	0	0	0	0	0	0	0	0	0	0	0	. 0	0
	750 ppm	0	0	0	0	0	0	0	Ō	0	0	õ	0	Õ	Ő
	1500 ppm	0	Ó	0	0	0	0	0	Õ	Ő	Ô	Ő	Ő	õ	Ő
	3000 ppm	0	0	0	Ō	0	Ő	Ő	õ	0 0	0	Ő	0 0	0	õ
EYE OPACITY	Control	1	1	1	1	I	1	1	1	1	1	1	1	1	1
	750 ppm	0	1	1	1	1	1	1	1	1	1	1	1	1	1
	1500 ppm	Ō	ō	Ō	ô	ō	ō	Ō	Ō	Ō	Ô	0	0	0	0
	3000 ppm	Ő	Ő	0	õ	õ	õ	0	0	0	0	0	0	0	0
CATARACT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ő	1	ĩ	1	1	1	1	1	1	1	1	1	1	1
	1500 ppm	0 0	Ô	0	Ô	Ô	0	0	0	0	0	0	0	-	-
	3000 ppm	0	0	0	0	0	0 0	0	0	0	0	0	0	0 0	0 0
CORNEAL OPACITY	Control	1	1	1	٦	1	1	1	1	1	1	1	1	1	1
	750 ppm	0	0	0	0	0	0	0	0	0	0	1	0	1	1
	1500 ppm	0	0	0	0	0	0	0	0	0	0	•	-	0	0
•	3000 ppm	0	0	0	0	0	0	0	0	•	-	0	0	0	0
		v	v	v	v	v	v	U	v	0	0	0	0	0	0
EXTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

STUDY NO. : 0267

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\sim$ 

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SEX : FEMALE

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

Clinical sign	Group Name	Admini	istration W	eek-dav											
	•	43-7	44-7	45-7	46-7	47-7	48-7	49-7	50-7	51-7	52-7	53-7	54-7	55-7	56-7
· · · · · · · · · · · · · · · · · · ·		-													
OSS OF HAIR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	Ő	0	Ő	õ
	1500 ppm	0	0	0	0	0	0	0	0	Õ	Õ	Õ	Ő	Õ	ŏ
	3000 ppm	0	0	0	0	0	0	Ő	Ő	Ő	Ő	Ő	0 0	0	0 0
OILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	Ö	0	õ	õ	ů 0	0	õ	Ő	0	0	0
	1500 ppm	Õ	õ	õ	õ	0	0	Ő	0	0	0	0	0	0	0
	3000 ppm	õ	õ	0	0	õ	0	0	0	0	2	0 2	0 3	0 3	0 1
XOPHTHALMOS	Control	1	1	1	1	1	1	1	1	I	1	1	1	1	,
	750 ppm	0	0	0	0	0	0	0	0	1	1	1	1	1	1
	1500 ppm	ŏ	0	0	0	0	0	0	0		-	0	0	0	0
	3000 ppm	0	0	0	0	0	0			0	0	0	0	0	0
	ann bbl	v	v	v	U	U	U	0	0	0	0	0	0	0	0
YE HEMORRHAGIC DISCHA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 maa	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EYE OPACITY	Control	1	1	1	1.	. 1	1	1	1	1	1	1	1	1	1
	750 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	ī
	1500 ppm	0	0	0	0	0 '	0	0	0	ō	2	2	2	2	2
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	ō	0	0
CATARACT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	1	1	1	1	1	1	1	1	ĩ	1	1	1	1	1
	1500 ppm	0	ō	ō	Ō	Ō	0	Ô	0	0	2	2	2	2	2
	3000 ppm	0	ő	Ő	õ	0	õ	0	0	0	0	0	0	0	0
ORNEAL OPACITY	Control	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	750 ppm	Ô	Ô	0	Ô	Ô	0	0	0	0	0	1	0	-	1
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0		0	0
	3000 ppm	Ő	o	Ő	0	0	0	0	0	0	0	0	0 0	0 0	0
EXTERNAL MASS	Control	0	٥	٥	0	4	•	<u>^</u>	•	•	•		-		
MILINAL MADD		0	0	0	0	1	0	0	0	0	0	0	0	0	0
	750 ppm	0	-	0	0	0	1	1	1	1	1	1	1	1	1
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

SEX : FEMALE

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

Clinical sign	Group Name																
		57-7	58-7	59-7	60-7	61-7	62-7	63-7	64-7	65-7	66-7	67–7	68-7	69-7	70-7		
										•							
OSS OF HAIR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
OILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	3000 ppm	1	1	1	1	1	1	2	2	2	2	2	1	1	1		
EXOPHTHALMOS	Control	1	1	1	1	1	1	1	1	1	1	1	1	1	1		
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
EYE HEMORRHAGIC DISCHA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ó		
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
EYE OPACITY	Control	1	1	1	2	2	2	2	2	2	2	2	2	2	2		
	750 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1		
	1500 ppm	2	2	2	2	2	2	2	2	2	2	2	2	2	2		
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
CATARACT	Control	0	0	0	1	1	1	1	1	1	1	1	1	1	1		
	750 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1		
	1500 ppm	2	2	2	2	2	2	2	2	2	2	2	2	2	2		
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	ō	õ		
CORNEAL OPACITY	Contral	1	1	1	1	1	1	1	1	1	1	1	1	1	1		
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	ō		
	1500 ppm	0	0	0	0	0	0	0	Ó	Ō	0 '	0	õ	Ő	Ő		
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	õ	Ő	0		
EXTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	750 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1		
	1500 ppm	0	0	0	0	0	Ō	1	1	1	ĩ	1	1	1	2		
	3000 ppm	0	0	0	0	0	Ó	ō	0	õ	ō	Ô	0	1	1		

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : FEMALE

Clinical sign	Group Name	Admini	stration W	leek-dav											
		71-7	727	73-7	74-7	757	76-7	77-7	787	79–7	80-7	81-7	82-7	83-7	84-7
OSS OF HAIR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	2	2
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	3	3
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	1
OILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	1	0	0	1	0	0	0	0	0	0	0	0	0	0
EXOPHTHALMOS	Control	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	750 ppm	0	0	0	0	0	0	0	0	Ō	0	Ō	0	0	Ô
	1500 ppm	0	0	0	0	0	0	0	0	Ō	Ō	Ō	0	Ō	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	õ	Ő
EYE HEMORRHAGIC DISCHA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	Ó	Ō	0
	mag 0008	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EYE OPACITY	Control	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	750 ppm	1	1	1	1	2	2	2	2	2	2	2	2	3	3
	1500 ppm	2	2	2	2	2	2	2	2	2	2	2	2	3	3
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CATARACT	Control	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	750 ppm	1	1	1	1	2	2	2	2	2	2	2	2	3	3
	1500 ppm	2	2	2	2	2	2	2	2	2	2	2	2	3	3
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ő	Ő
CORNEAL OPACITY	Control	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	750 ppm	0	0	0	0	0	0	0	0	Ō	0	õ	0	0	Ô
	1500 ppm	0	0	0	0	0	0	0	0	Ō	õ	õ	Ő	ů	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	· 0	Ő	Ő
EXTERNAL MASS	Control	0	1	1	2	1	1	1	1	1	1	1	2	3	3
	750 ppm	1	1	1	2	2	2	2	2	2	3	3	3	4	4
	1500 ppm	2	1	1	1	1	1	1	1	1	2	3	2	4	4
	3000 ppm	1	1	1	ō	0	0	ō	1	1	1	2	2	2	2

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS -\_\_\_\_\_

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SEX : FEMALE

Clinical sign	Group Name	Admini	stration W	leek-dav											
		85-7	86-7	87-7	88-7	89-7	907	91-7	927	93-7	94-7	95-7	96-7	97-7	98-7
								· • • • • • • • • • • • • • • • • • • •							
OSS OF HAIR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	2	2	2	2	2	2	2	2	3	3	3	3	3	ů 3
	1500 ppm	2	2	2	2	2	2	2	2	3	3	3	3	3	4
	3000 ppm	1	1	1	1	1	1	1	1	1	1	2	2	2	2
DILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	1	1
	750 ppm	1	0	0	0	0	0	0	0	0	õ	õ	õ	Ô	Ô
	1500 ppm	0	0	0	0	Ō	0	õ	Õ	õ	õ	õ	0	0	0
	3000 ppm	0	0	õ	Ő	ő	0	0	0	Ŏ	0	0	0	0	0
XOPHTHALMOS	Control	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	750 ppm	0	0	0	ō	Ō	Ō	ō	0	0	0	0	0		1
	1500 ppm	õ	0 0	Ő	0	Ő	0	0	0	0	0	0		0	0
	3000 ppm	õ	ő	0	0	0	0	0	0	0	0	0	0 0	0 0	0 0
EYE HEMORRHAGIC DISCHA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	Õ	Õ	Ő	0	ŏ	0	0	0	1	-	-	0
	1500 ppm	Õ	Ő	0	Ő	0	0	0	0	0	0	-	1	1	1
	3000 ppm	0	Ő	0	0	0	0	0	0	0	0	0 0	0	0 0	0 0
YE OPACITY	Control	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	750 ppm	3	3	3	-3	3	3	3	3	3	3	3	3	23	
	1500 ppm	4	4	4	4	4	4	4	4	4	4	4	4		3
	3000 ppm	ō	Ō	ō	ō	0	0	0	0	0	0	4 1	4 1	4 1	$\frac{3}{1}$
ATARACT	Control	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	750 ppm	3	3	3	3	3	3	3	3	3	3	3	3	3	-
	1500 ppm	4	4	4	4	4	4	4	4	4	4	3 4	4		3
	3000 ppm	ō	Ō	0	0	0	0	0	0	4	4	4	4	4 1	3 1
ORNEAL OPACITY	Control	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	750 ppm	0	0	ō	ō	0	Ô	Ô	0	0	0	0	0	0	1
	1500 ppm	õ	0	õ	õ	0	0	0	0	0	0	0	0		0
	3000 ppm	Ő	õ	õ	0 0	0	0	0	0	0	0	0	0	0 0	0 0
EXTERNAL MASS	Control	3	3	3	3	4	4	4	4	5	5	5	5	6	7
	750 ppm	5	5	5	6	7	6	4 6	6	6	5 6	5 5			
	1500 ppm	4	4	5	5	5	5	7	7	o 7	ь 6		6	6	7
	3000 ppm	1	1	1	1	1	J 1	1	1			8	8	8	8
		*	1	T	1	T	Ť	L	T	1	1	1	1	1	3

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\sim$ 

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### SEX : FEMALE

LOSS OF HAIR	Group Name	99-7	istration N 100-7	101-7			
LOSS OF HAIR					102-7	103-7	104-7
LOSS OF HAIR							101 1
LOSS OF HAIR							
LUSS OF HAIR	<b>a</b>						
	Control	0	0	0	0	0	0
	750 ppm	3	3	3	3	3	3
	1500 ppm	4	3	3	3	3	4
	3000 ppm	2	3	3	3	3	2
OILED PERI GENITALIA	Control	0	0	0	0	0	0
	750 ppm	Ő	Ő	0	0	0	0
	1500 ppm	Ő	0	0	0	Ő	
	3000 ppm	0	0	0	0		0
		v	v	U	0	0	0
XOPHTHALMOS	Control	1	1	1	1	1	1
	750 ppm	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0
EYE HEMORRHAGIC DISCHA	Control	٥	0	0	^	•	•
TE HERORAHAGIO DISORA	Control	0	-		0	0	0
	750 ppm	1	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0
YE OPACITY	Control	3	3	3	3	3	2
	750 ppm	3	3	3	3	3	3
	1500 ppm	3	3	3	3	3	3
	3000 ppm	1	1	1	1	1	1
ATARACT	0			_	_	-	
ATANAUI	Control	1	1	1	1	1	1
	750 ppm	3	3	3	3	3	3
	1500 ppm	3	3	3	3	3	3
	3000 ppm	1	1	1	1	1	1
RNEAL OPACITY	Control	2	2	2	2	2	1
	750 ppm	0	0	0	0	0	0
	1500 ppm	0	0	0	0		
	3000 ppm	0	0	0	0	0	0
		v	v	v	v	0	0
EXTERNAL MASS	Control	7	9	10	9	7	7
	750 ppm	7	8	9	10	12	14
	1500 ppm	9	8	8	8	7	8
	3000 ppm	3	4	4	4	5	5

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\sim$ 

SEX : FEMALE

Clinical sign	Group Name	Admini	stration We	eek-day			•								······
	-	1–7	2–7	3-7	4-7	5-7	6-7	7–7	8-7	9–7	10-7	11-7	12-7	13-7	14-7
	<b>A</b>	_													
INTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M.PERI MOUTH	Contract	ò	^	0	<u>^</u>	•	•								
A.FEAT MOOTH	Control 750 and	0	0	0	0	0	0	0	0	0	0	0	0		0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0		0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0		0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M.ORAL CAVITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	^	٥
	750 ppm	0	õ	ŏ	Õ	õ	0	0 0	0	0	0	0	0		0
	1500 ppm	Ō	Ő	Õ	ŏ	õ	õ	õ	Ő	õ	0	0	0		0
	3000 ppm	0	0	Ō	õ	õ	Ő	õ	0	0	0 0	0	0		0
												•	Ū	v	v
M.EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M.PERI EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	٥
	750 ppm	ŏ	õ	ŏ	õ	0	0 0	õ	0	0	0	0	0	0	0
	1500 ppm	0	Õ	Õ	õ	Ő	ŏ	ŏ	Ő	0	0	0	0	0	0
	3000 ppm	0	Õ	Õ	õ	Ő	Ő	Ő	0	0	0	0	0	0	0
M.HEAD				_									Ť	v	Ū
A. HEAD	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M.BREAST	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	٥
	750 ppm	0	0	Ő	õ	õ	õ	õ	0 0	0	0	õ	0	•	0
	1500 ppm	õ	õ	ŏ	Ő	0 0	0	0	0	0	0	0	0	0 0	0
	3000 ppm	0	Ō	Ō	Ō	õ	Ő	Õ	õ	0	0	0	0	0	0
A PROVEN				_								-	-		v
M. ABDOMEN	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\sim$ 

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SEX : FEMALE

Clinical sign	Group Name	Admini	stration W	eek-dav											
_		15-7	16-7	17-7	18-7	19–7	20-7	21-7	22-7	23-7	24-7	25-7	26-7	27-7	28-7
								- /	·····						
NTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	õ	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ő	Õ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Õ
.PERI MOUTH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	Ō	Ő	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Õ	Ő
I.ORAL CAVITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	Ō	Ő	õ	õ	Ő
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Õ	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Õ	Ő
EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	Ō	0	õ	0	ů	Ő	Ő
	1500 ppm	0	0	0	0	0	0	0	Ō	0	Ő	Ő	0 0	õ	0 0
	3000 ppm	0	0	0	0	0	0	0	0	0	Ō	Ő	Ő	ő	Ő
.PERI EAR	Control	0	0	0	0	. 0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	õ	ŏ
	1500 ppm	0	0	0	0	0	0	0	0	0	Ó	0	Õ	Ő	Õ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	õ
I.HEAD	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ő	Õ
	1500 ppm	0	0	0	0	0	0	0	0	Ó	0	0	Ő	Ő	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	Õ	Õ	Ő
1.BREAST	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	Ō	Ő	Õ	Ő	õ	ŏ	0 0
	1500 ppm	0	0	0	0	0	Ō	0	õ	õ	õ	Ő	Ő	ŏ	ŏ
	3000 ppm	0	0	0	0	0	0	0	0	0	õ	Ő	Ő	Õ	0
ABDOMEN	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	õ	Õ	õ	ŏ	0
	1500 ppm	0	0	0	0	0	0	0	Õ	Õ	õ	0	Ő	õ	0
	3000 ppm	0	0	0	0	0	0	0	0	Ō	0	0	ů	õ	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS · ----

SEX : FEMALE

Clinical sign	Group Name	Admini	stration W	eek-dav											
	-	29-7	30-7	31-7	32-7	33-7	34-7	35-7	367	37-7	38-7	39-7	40-7	41-7	42-7
NTERNAL MASS	Constant.	â	<u>^</u>						_						
NIERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PERI MOUTH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Õ
.ORAL CAVITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	Ő	Ő	Ő	Ő	Ő	0	0	0 0	0	0
	1500 ppm	0	0	Ő	Õ	0	Ő	Ő	ŏ	õ	õ	õ	0	0	0
	3000 ppm	0	0	Ō	Ő	Ő	õ	Ő	0	Ő	0	0	0	0	0
LEAR	Contral	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ő	õ	õ	0	0	õ	0	0	0	0	0	0	0	•
	1500 ppm	õ	õ	0	0	ŏ	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0 0	0
I.PERI EAR	Control	0	0	0	0	0	0	0	0	0	0	0		0	0
	750 ppm	õ	õ	0	Ő	Ő	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
HEAD	Control	0	0	0	0	0	0	0	^	<u>^</u>					
	750 ppm	Õ	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0				0	0	0	0	0	0	0	0
		0	-		0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
I.BREAST	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Õ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	Ő	Ő	Ő
ABDOMEN	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	Ō	Õ	Õ	Ő	0	Ő	õ	õ	õ	õ	õ	0
	1500 ppm	0	0	0	õ	Ő	0	õ	Ő	Ő	0	0	0	0	•
	3000 ppm	ů	Ő	Ő	0 0	0	0	0	0	0	0	0	0	0	0 0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS . ب

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SEX : FEMALE

Clinical sign	Group Name														
		43-7	stration W 44-7	45-7	46-7	47-7	48-7	49-7	50-7	51-7	52-7	53-7	54-7	55-7	56-7
TERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0.	0	0	0	0	0	0	0	0	0	0	0	0	0
PERI MOUTH	Control	0	0	0	0	1	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	Ő	õ	Õ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Õ	Ő
.ORAL CAVITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	Õ	Ō	Õ	õ	Ő
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Õ	Õ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	Ő	õ	Ő
EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	Ó	Ō	0	õ	Õ
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Õ	Õ	Ő	ő
	3000 ppm	0	0	0	0	0	0	0	õ	õ	0	õ	õ	ů ·	õ
.PERI EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	1	1	1	1	1	1	1	1	1
	1500 ppm	0	0	0	0	0	0	ō	ō	ō	ō	ō	ō	ō	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	Ő	õ	õ	Ő
I.HEAD	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	Ō	0	· 0	õ	Ő	Õ	õ	0	Ő	õ
	1500 ppm	0	0	0	0	Õ	õ	õ	õ	õ	õ	ů 0	0	Ő	0
	3000 ppm	0	0	0	0	0	0	0	Ő	õ	õ	õ	Ő	0	ŏ
I. BREAST	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	Ō	0	Ő	0	0	0	õ	Õ	0	0	0
	1500 ppm	Ö	õ	õ	ŏ	ŏ	, Õ	Ö	õ	0	0.	0	0	Ő	0
	3000 ppm	0	0	õ	Ő	õ	0	0	õ	0	ŏ	0	0	0	0
. ABDOMEN	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ő	0	õ	Ő	ŏ	õ	õ	õ	õ	õ	0	0	0	0
	1500 ppm	õ	õ	Ő	õ	Õ	Ő	0	0	0	0	0	0	0	0
	3000 ppm	ů	Ő	õ	õ	ŏ	õ	Ő	0	0	0	0	0	0	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : FEMALE

Clinical sign	Group Name	Admini	stration W	eek-day				±							
	· · · · · · · · · · · · · · · · · · ·	577	58-7	59-7	60-7	61-7	62-7	637	64-7	65-7	66-7	67-7	68-7	69-7	70-7
NTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PERI MOUTH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
.ORAL CAVITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	Õ	0	õ	õ	õ	Ő	õ	Ő	õ	Ő	0
	1500 ppm	0	0	0	0	0	0	0	Ő	0	Õ	Ő	Ô	ő	õ
	3000 ppm	0	0	0	0	0	0	0	õ	Õ	Õ	Ő	Ő	Õ	0
.EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ō	0	0	Õ	Ő	Õ	õ	õ	Ő	õ	õ	Ő	Õ	0
	1500 ppm	Õ	Ő	Õ	õ	õ	Ő	õ	Ő	0	0	õ	õ	õ	0
	3000 ppm	Õ	Ő	õ	0	õ	0 0	õ	0	0 0	õ	0	0	0	0
.PERI EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	1500 ppm	Ō	Ō	ō	0	Ô	Ô	Ō	Ô	Ô	0	0	0	0	0
	3000 ppm	0	õ	Ő	Ő	Ő	Ő	õ	0	õ	0 0	0	0	0	0
HEAD	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	ŏ	0	0	0	0	0	0 0	0	0	0	0	0	0	0
	1500 ppm	Ő	0	0	0	0 0	0	0	0	0	0	0	0	0	0
	3000 ppm	Ő	0	0	0	0	0	0	0	0	0	0	0	0	0
BREAST	Control	0	0	0	0	0	0	0	0	0	0	0	٥	^	0
	750 ppm	0	0	0	0	0	0	0	0		-	•	0	0	. 0
	1500 ppm	0	0	0	0	0	0	0		0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	1	1	1	1	1	1	1	1
	SUUU PPM	v	v	v	U	v	U	U	0	0	0	0	0	0	0
ABDOMEN	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : FEMALE

Clinical sign	Group Name	AQMINI	stration W	еек-дау											
		71-7	72-7	73-7	74-7	75-7	76-7	77-7	787	79-7	80-7	81-7	82-7	83-7	84-7
NTERNAL MASS	Control	0	0	0	٥	٥	0	0	0	0	â	•	•		
MILMML INDO	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0			-		-	0	0	0	0	0	1
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppili	U	0	U	U	0	0	0	0	0	0	0	0	0	0
PERI MOUTH	Control	0	1	1	1	0	0	0	0	0	0	0	0	0	٨
	750 ppm	Ő	Ō	0	0	0	0	0	0	0	0	0	0	-	0
	1500 ppm	ŏ	0	0	0	0	0	0		-		•	•	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		U	U	U	U	U	U	U	0	0	0	0	0	0	0
I.ORAL CAVITY	Control	0	0	0	0	0	0	0	0.	0	0	0	0	0	0
	750 ppm	Õ	0 0	õ	õ	Õ	0	õ	0 0	õ	0	0	0	0	0
	1500 ppm	Ő	ő	Ő	õ	Ő	õ	õ	ŏ	0	ŏ	0	0	0	0
	3000 ppm	Ő	0	Ő	õ	0	Ő	0	0 0	0	0	0	0	0	
		v	v	v	U	v	v	v	v	U	v	U	U	U	0
.EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	Ō	0	0	Õ	Ő	1	1	1	1	1	1	1
	1500 ppm	0	Ō	Õ	õ	Õ	õ	Ő	Ô	0	Ô	Ô	0	0	0
	3000 ppm	0	0	0	Õ	õ	Õ	õ	õ	õ	õ	0	0	ŏ	0
DEDT DID				•											
.PERI EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	1	1	1	1	1	1	1	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
.HEAD	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	Ō	Ö	õ	õ	Ő	õ	Ő	Õ	õ	0	0	0	0
	1500 ppm	1	Õ	Õ	õ	Ő	ŏ	õ	0	0	Ő	0	0	0	
	3000 ppm	0	õ	0	0	0	õ	0	0	0	0	0	0	0	0
		v	v	v	v	v	v	v	U	U	U	U	U	U	U
BREAST	Control	0	0	0	0	0	0	0	0	0	0	0	1	1	1
	750 ppm	0	0	Ő	Ő	Õ	Ő	Ő	ů	õ	Õ	0	0	0	0
	1500 ppm	1	ĩ	1	1	1	1	1	1	1	1	1	1	1	1
	3000 ppm	Ô	0	0	0	0	0	0	1	1	1	1	1	1	1
		v	v	v	v	v	v	v	Ŧ	T	T	1	T	T	1
(. ABDOMEN	Control	0	0	0	0	0	0	0	0	0	0	0	0	1	1
	750 ppm	0	0	0	0	0	0	0	0	Ō	0	Õ	õ	1	1
	1500 ppm	0	0	0	0	0	Õ	Ö	õ	õ	ů	õ	Ő	1	1
	3000 ppm	0	0	Õ	0	Ő	Õ	Ő	õ	Ő	Õ	Ő	0	0	0 0

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104 CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS . \_\_\_\_

SEX : FEMALE

Clinical sign	Group Name	Admini	stration W	eek∽dav											
		85-7	86-7	87-7	88-7	89-7	907	91-7	92-7	937	94-7	95-7	96-7	97-7	987
NTERNAL MASS	Control	0	0	0	0	0	0	1	1	1	1	2	4	4	3
	750 ppm	1	0	0	0	0	0	0	1	1	1	1	1	1	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	ō	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PERI MOUTH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	1	2	2	2	1	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	1	1	1	0	1	1	1	1
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	Ō	ō	ō
I.ORAL CAVITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ő	ŏ
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ó	Ö
	3000 ppm	0	0	0	0	0	0	0	0	0	0	Ō	Õ	õ	Ő
I.EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	1	1	1	1	0	0	0	0	0	0	Ó	ō	õ	õ
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	Ō	õ	Ő
	3000 maa	0	0	0	0	0	0	0	0	0	0	0	0	0	0
I.PERI EAR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	1	0	0	0	0	0	0	0	0	Ó
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
f.HEAD	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
.BREAST	Control	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	750 ppm	0	0	0	0	0	1	1	1	1	1	1	1	î	1
	1500 ppm	1	1	2	2	2	2	2	2	2	2	2	2	2	2
	3000 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
LABDOMEN	Control	1	1	1	1	1	1	1	1	2	2	2	2	3	3
	750 ppm	1	1	1	2	2	2	2	2	2	2	2	2	2	1
	1500 ppm	1	1	1	1	1	1	1	1	1	1	2	2	2	2
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	õ	õ

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : FEMALE

Clinical sign Group Name Administration Week-day \_ 99-7 100-7 101-7 102-7 103-7 104-7 INTERNAL MASS Control 750 ppm 1500 ppm 3000 ppm M.PERI MOUTH Contral 750 ppm 1500 ppm 3000 ppm M.ORAL CAVITY Control 750 ppm 1500 ppm 3000 ppm M.EAR Contral 750 ppm 1500 ppm 3000 ppm M.PERI EAR Control 750 ppm 1500 ppm 3000 ppm M.HEAD Control 750 ppm 1500 ppm 3000 ppm M.BREAST Control 750 ppm 1500 ppm 3000 ppm M. ABDOMEN Control 750 ppm 1500 ppm 3000 ppm 

(HAN190)

(HAN190)

STUDY NO. :	0267
ANIMAL :	RAT F344/DuCrj
REPORT TYPE	: A1 104

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS ~

SEX : FEMALE

linical sign	Group Name	Adminis	stration We	ek∽dav											
•	• · · · · · · · · · · · · · · · · · · ·	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	147
ANTERIOR.DORSUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
HINDLIMB	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ő
I.GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	õ	õ	Ő	õ
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Õ	Õ
	3000 ppm	0	0	0	0	0	0	0	0	Ő	Ő	Ő	Ő	õ	Ő
I.TAIL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ó	0	0	Ő	õ	Ő	õ	ů 0	õ	0 0	0 0	ŏ	0	0
	1500 ppm	Õ	Õ	õ	Ő	õ	õ	0 0	0	Ö	0 0	0	0	0	0
	3000 ppm	Ö	0	õ	Ő	0	0	0	0	0	0	0	0	0	0
NEMIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	. 0	0
	750 ppm	0	0	0	Ö	Ō	Õ	Ő	Ő	õ	õ	õ	0	0	0
	1500 ppm	Õ	Ő	õ	Ő	õ	õ	ŏ	õ	0	õ	0	Ő	0	0
	3000 ppm	Ō	0	õ	Ő	0	õ	Õ	õ	0	õ	0	0	0	0
IAUNDISE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	õ	õ	Õ	Ö	0 0	ŏ	õ	õ	0	0	0 0	0	0
	1500 ppm	õ	õ	õ	õ	õ	0	õ	0	0	0	0	0	0	. 0
	3000 ppm	Ő	õ	0	0	0	0	0	0	0	0	0	0	0	0
CRUSTA	Contral	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ő	õ	Ő	Õ	Ö	0	õ	0	0	0	0	•		-
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	v	•	0	0
		v	v	v	v	v	v	v	v	U	U	0	0	0	0
SWELLING	Control	0	0	0	0	0	0	0	0	0	0	0	0.	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Õ	Õ
	1500 ppm	0	0	0	0	0	0	0	Ō	Ō	Õ	Õ	õ	0 0	0 0
	3000 ppm	0	Ö	0	0	Ō	Õ	Ő	Õ	õ	Ő	õ	0	0	0

PAGE : 73

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\sim$ 

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SEX : FEMALE

Clinical sign	Group Name	Admini	stration W	eek-dav											
		15-7	16-7	17-7	187	19-7	20-7	21-7	22-7	23-7	24-7	25-7	26-7	27-7	28-7
.ANTERIOR.DORSUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	Ō	0	0	Ő	õ	õ
	1500 ppm	0	0	0	0	0	0	0	0	0	0	õ	0	ů	Õ
	3000 ppm	0	0	0	0	0	0	0	0	Ő	Ő	0	Ő	Ő	0
.HINDLIMB	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	Ő	Ō	Ő	õ	Ő	Õ	0	0	0
	1500 ppm	0	0	0	0	Ő	õ	ů	Ő	Ő	Ő	0	0	Ő	
	3000 ppm	0	0	õ	ő	õ	õ	0	0	õ	õ	0	0	0	0 0
GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ő	õ	õ	Ő	0	0	0	Ő	0	0	0	•	0	0
	1500 ppm	Ő	ŏ	0	0	õ	0	0	0			-	0	0	0
	3000 ppm	0	0	õ	0	ŏ	0	0	0	0	0	0	0	0	0
							-		v	v	v	v	v	U	v
.TAIL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
NEMIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	- 0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Õ	õ	ŏ	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	õ	õ	Ő	Ő
AUNDISE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	õ	Õ	õ	Õ	. 0	0 0	0	0	0
	1500 ppm	0	0	0	0	õ	Õ	Ő	0	0	0	ŏ	0	0	
	3000 ppm	õ	Õ	ŏ	ő	õ	0	0	0	0	0	0	0	0	0 0
RUSTA	Control	0	0	0	0	0	0	0	0	0	0	0	0	٥	0
	750 ppm	Õ	õ	õ	Ő	0	Ő	0	0	0	0	0	•	0	0
	1500 ppm	ŏ	0	0	0	0	0	0	0	0	0		0	0	0
	3000 ppm	0	õ	õ	0	0	0	0	0	0	0	0	0	0	0 0
WELLING	Control	0	0	0	^	0	0	0	<u>^</u>				-	-	
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		-	•	-	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\sim$ 

SEX : FEMALE

Clinical sign	Group Name	Admini	stration W	eek-dav											
		29-7	30-7	31-7	32-7	33-7	34-7	35-7	36-7	37-7	38-7	39-7	40-7	41-7	42-7
ANTERIOR.DORSUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
.HINDLIMB	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
I.GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Õ
I,TAIL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Ő	Ő	Õ
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Õ	Õ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ő	õ
NENIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0 -
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ō
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
JAUNDISE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ō
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	Ō	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ő
RUSTA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Õ	õ	õ
	1500 ppm	0	0	0	0	0	Ō	0	0	Õ	õ	Ő	õ	ů	0 0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
WELLING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	Ő	Õ	Ő	Ő
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Ő	Ő	õ	õ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	Ő	õ	õ

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS · \_\_\_\_ ·

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SEX : FEMALE

Clinical sign	Group Name	Admini	stration W	eek-day											
		43-7	44-7	45-7	46-7	47-7	48-7	49-7	50-7	51-7	52-7	53-7	54-7	55-7	56-7
.ANTERIOR.DORSUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
.HINDLIMB	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	Ő	Ō	0	0	Ō
	1500 ppm	0	0	0	0	0	0	0	0	Ó	0	0	Ô	Ő	õ
	3000 ppm	0	0	0	0	õ	õ	Õ	õ	õ	0	0	õ	ő	ŏ
GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	õ	Ő	Õ	õ	Õ	õ	0	ŏ
	1500 ppm	Ō	Ő	Õ	Õ	Õ	Ö	õ	Ő	Ő	õ	õ	0	0	0
	3000 ppm	Ő	Õ	õ	õ	0	ő	õ	0	0	ŏ	0 0	0 0	0	0
.TAIL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	Ō	Ő	Õ	ů.	Ő	0	0
	1500 ppm	Ó	0	ō	0	Õ	Õ	õ	õ	Õ	õ	Ő	0	0	0
	3000 ppm	0	0	0	õ	õ	õ	õ	õ	0	Ő	õ	0	0	0
NEMIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	õ	0	Õ	õ
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	Ō	Ō	Õ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	Ō	Ő	õ
AUNDISE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Ő	0	Ő
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Õ	Õ	Ő	õ
	3000 ppm	0	0	0	0	0	Ō	0	õ	Õ	õ	0	0	0 0	õ
CRUSTA	Contral	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	Ő	õ	Ő	Ő	õ	Ő	Ő	0
	1500 ppm	0	0	0	Ö	Õ	1	1	1	1	ĩ	1	2	2	2
	3000 ppm	0	0	õ	Ő	Ö	ō	ō	0	0	0	0	0	0	0
WELLING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	Ō	Ő	Õ	õ	õ
	1500 ppm	0	0	0	0	0	Ō	Õ	Õ	Õ	Ő	õ	õ	0	Ő
	3000 ppm	0	Ō	Ō	0	0	Ő	Õ	õ	Ő	õ	0 0	0	0	0

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

SEX : FEMALE

Clinical sign	Group Name	Admini	stration W	eek-day											
		57-7	58-7	59-7	60-7	61-7	62-7	63-7	64-7	657	66-7	677	68-7	69-7	70-7
ANTERIOR DORSUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
.HINDLIMB	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
I.GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	Ō	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Ó	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	1
I.TAIL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	Ó	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ō	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
NEMIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0 0	0	Õ
	1500 ppm	0	0	0	0	0	0	0	Ó	0	Ō	0	Õ	0	Õ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
JAUNDISE	Control	0	0	0	0	0	0	0.	0	0	0	0	0	0	0
	750 ppm	0	0	0	Ō	0	Õ	0	õ	õ	Õ	Ô	õ	0	õ
	1500 ppm	Ó	0	Ō	0	Ő	Ő	Õ	õ	õ	0	Õ	0	0	ŏ
	3000 ppm	0	0	Õ	Ő	Õ	õ	õ	Ő	õ	0	0 0	õ	0	0
CRUSTA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	õ	õ	Ő	ŏ	õ	Õ	0	ŏ	0	0	0	0	0	0
	1500 ppm	2	2	4	4	4	4	4	4	4	4	4	0 5	5	5
	3000 ppm	0	õ	ō	0	ō	Ō	0	0	0	0	0	0	0	0
SWELLING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	õ	Ő	ů 0	õ	õ	ŏ	0	õ	0	0	0	0	0	0
	3000 ppm	õ	õ	õ	õ	õ	õ	õ	0	õ	0	0	0	0	0

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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REPORT	TYPE	:	Å1	104	

SEX : FEMALE

Clinical sign	Group Name	Admini	stration W	eek-dav											
		71-7	72-7	73-7	74-7	75-7	76-7	77-7	787	79–7	80-7	81-7	82-7	83-7	84-7
.ANTERIOR.DORSUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ő
HINDLIMB	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	Ō	0	0	Ő	Ő	õ	Õ	ŏ
	3000 ppm	0	0	0	0	0	0	õ	0	õ	Ő	õ	õ	Ő	õ
.GENITALIA	Control	0	0	0	1	1	1	1	1	1	1	1	1	1	1
	750 ppm	0	0	0	1	1	1	1	1	1	2	2	2	2	2
	1500 ppm	0	0	0	0	0	0	0	ō	ō	1	1	1	2	2
	3000 ppm	1	1	1	0	0	0	0	Ő	Ö	õ	1	1	1	1
.TAIL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ō
	1500 ppm	0	0	0	0	0	0	0	0	0	0	1	0	Õ	Õ
	3000 ppm	0	0	0	0	0	0	0	0	0	õ	õ	õ	õ	õ
NEMIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	1	0	0	0	0	0	0	0	. 0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
IAUNDISE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ō
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ő
RUSTA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	1	1	1	1	1	2	2	1	1	1	ĩ	1	1
	1500 ppm	5	5	5	5	5	5	5	5	5	5	5	5	6	6
	3000 ppm	0	0	0	0	õ	0	1	1	1	1	1	1	1	1
WELLING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	Ō	Ō	Ő	0	ů	Ő	Ő	Ő
	1500 ppm	0	0	0	0	1	0	1	1	1	1	1	1	1	1
	3000 ppm	Ō	Õ	0	õ	Ô	Õ	Ô	0	Ô	0	0	0	0	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : FEMALE

Clinical sign	Group Name	Admini	stration W	eek-day											
		85-7	86-7	87-7	88-7	89-7	90-7	91-7	92-7	93–7	94-7	95-7	96-7	977	98-7
ANTERIOR.DORSUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	1500 ppm	0	0	0	0	0	0	1	1	1	1	1	1	1	1
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	1
HINDLIMB	Contral	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
I.GENITALIA	Control	1	1	1	1	2	2	2	2	2	2	2	2	2	3
	750 ppm	2	2	2	2	3	3	3	3	3	3	2	3	3	4
	1500 ppm	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	3000 ppm	0	0	0	0	0	0	0	0	0	0	Ō	0	ō	1
.TAIL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	Ō	0	Ő	Ő
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
NEMIA	Control	0	0	0	0	0	0	0	0	0	0	2	0	1	0
	750 ppm	0	0	0	0	0	0	0	0	1	1	1	1	1	Ó
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ō
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
JAUNDISE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CRUSTA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	1	1	1	2	2	2	2	2	2	2	ž	2	2 2	2
	1500 ppm	6	6	6	6	6	6	6	6	6	6	6	6	7	7
	3000 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
SWELLING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	Ō	Ō	Ő	ŏ	õ	õ	0
	1500 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	3000 ppm	0	0	0	0	0	0	0	0	0	ō	0	Ō	ô	Ô

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS ~

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SEX : FEMALE

PAGE : 80

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Clinical sign	Group Name	Admin	istration	Week-day				 	 	
-		99-7	100-7	101-7	102-7	103-7	104-7	 		 
ANTERIOR.DORSUM	Control	0	0	0	1	1	1			
	750 ppm	1	1	1	1	3	3			
	1500 ppm	1	1	1	1	1	1			
	3000 ppm	1	1	ĩ	1	2	2			
4.HINDLIMB	Cantanal	٥	0	٥	٥	•	0			
A. HINDLIND	Control	0	0	0	0	0	0			
	750 ppm	0	1	1	1	1	1			
	1500 ppm	0	0	0	0	0	0			
	3000 ppm	0	0	0	0	0	0			
M.GENITALIA	Control	3	4	4	3	3	3			
	750 ppm	4	4	3	3	3	4			
	1500 ppm	2	3	3	3	2	3			
	3000 ppm	1	2	2	2	4	0			
		1	2	4	Z	2	2			
M.TAIL	Contral	0	0	0	0	0	0			
	750 ppm	0	0	0	0	0	0			
	1500 ppm	0	0	0	0	0	0			
	3000 ppm	0	0	0	0	0	0			
ANEMIA	Control	0	0	1	1	0	0			
	750 ppm	Ő	Õ	î	1	õ	õ			
	1500 ppm	1	ŏ	0	0	0				
			0				0			
	3000 maa	0	0	0	0	0	1			
JAUNDISE	Control	0	0	0	0	1	1			
	750 ppm	0	0	0	0	0	0			
	1500 ppm	0	0	0	0	0	0			
	3000 ppm	0	0	0	0	0	0			
CRUSTA	Control	0	0	0	0	0	0			
	750 ppm	2	2	2						
					2	2	2			
	1500 ppm	7	7	7	7	7	7			
	3000 ppm	1	1	1	0	0	0			
SWELLING	Control	0	0	0	0	0	0			
	750 ppm	0	0	0	0	0	0			
	1500 ppm	1	1	1	1	1	1			
	3000 ppm	ō	ō	ô	Ō	Ô	ō			
		v	v	v	v	v	v			

STUDY NO. :	0267
ANIMAL :	RAT F344/DuCrj
REPORT TYPE	: A1 104

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS `~~~

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SEX : FEMALE

Clinical sign	Group Name	Admini	stration We	əek-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	137	14-7
EMORRHAGE	Cantural	0	•	0	•	•	0								
LIOAAIAGE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0 .	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DRTICOLLIS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	. 0	0	0	0
	1500 ppm	0	0	0	0	0	0	Ō	0	Õ	Õ	Õ	õ	õ	õ
	3000 ppm	0	0	0	0	0	0	õ	õ	õ	õ	õ	Õ	Ő	0 0
RREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	õ	õ	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	-	•	-			0
	3000 ppm	0	0	0	0	0	0	0	•	0	0	0	0	0	0
		v	v	v	U	v	v	U	0	0	0	0	0	0	0
SNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
BNORMAL RESPIRA.SOUND	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	Ó	0	Ő	0	0	0	Ő	õ	Õ	0
	1500 ppm	0	0	Ö	0	Ō	Õ	õ	õ	õ	0	Ő	ŏ	Ő	0
	3000 ppm	0	0	0	Ō	Õ	Ő	õ	õ	õ	õ	õ	õ	ŏ	0
EMATURIA	Control	0	0	0	0	٥	٥	0	0	0	•	•	<u>^</u>		
	750 ppm	0	0	0	0	0 0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0				-	-	0	0	0	0	0	0
		•	-	-	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ED URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ő
	1500 ppm	0	0	0	0	0	0	0	0	Ō	Õ	Õ	õ	Õ	0
	3000 ppm	0	0	0	0	0	0	0	0	0	õ	Ő	Õ	0	Ů
ELLOW URINE	Control	0	0.	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ő	0	Ő	Ő	Ő	Õ	õ	õ	õ	Ő	0	0	0	0
	1500 ppm	0	õ	0	0	0	0	0	0	0	0	0	0	0	•
	3000 ppm	Ő	Ő	0	0	0	0	0	0	0	0	0	0	0	0

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

## SEX : FEMALE

Clinical sign	Group Name	Admini	stration W	eek-dav											
		15–7	16-7	17-7	18-7	19-7	20-7	21-7	22-7	23-7	24-7	25-7	26-7	27-7	28-7
IEMORRHAGE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	õ	Ő	ő	Ő
ORTICOLLIS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Ō	0	0	Õ
	3000 ppm	0	0	0	0	0	0	0	0	0	õ	õ	Ő	õ	0
RREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	Ő	0	0	Ő	Ő	Ő
	1500 ppm	0	0	0	0	Ō	Ō	Ő	Õ	õ	õ	Ő	Ő	0	Ő
	3000 ppm	0	0	0	0	0	0	Õ	õ	õ	õ	0	õ	0	0
BNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	Ō	0	0	Ő	0	Ő	Ő	Ő
	1500 ppm	Ō	0	õ	Õ	Õ	Ő	õ	0	õ	0 0	0	0	0	ő
	3000 mag	Ő	Õ	0	õ	0	0	õ	õ	0	0	0	0	0	0
BNORMAL RESPIRA.SOUND	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	Ő	Ō	Ő	õ	Õ	0	õ	0	õ
	1500 ppm	0	Ö	Ō	0	Õ	Õ	õ	õ	0	0	0	0	ŏ	0
	3000 ppm	0	0	0	0	õ	Ő	õ	õ	Ő	Õ	0	0	0 0	0
EMATURIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	Õ	Ő	Õ	õ	Õ	0	Ő	0	0
	1500 ppm	0	0	Ō	Õ	Ő	õ	õ	Ő	õ	0	0	0	0	0
	3000 ppm	Ő	Õ	0	ő	ő	õ	õ	0	0	0	0	0	0	0
ED URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	õ	õ	0	õ	Ö	Ő	Ő	0 0
	1500 ppm	Ō	0	0	0	õ	õ	ů 0	õ	õ	0	0	Ő	0	. 0
	3000 ppm	0	0	0	0	õ	õ	Õ	ő	0	õ	0	0 0	õ	0
ELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	Ő	0	Ő	Õ	Õ	õ	õ	0	0	õ	Ő	Ő	0
	1500 ppm	õ	Õ	õ	Ő	0	Ö	Ő	0	0	0	0	0	0	0
	3000 ppm	õ	Ő	ů	Õ	Ő	0	0	0	0	0	0	0	0	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : FEMALE

Clinical sign	Group Name	Admini	stration W	leek-dav											
-		29-7	30-7	31-7	32-7	33-7	34-7	35-7	36-7	37-7	38-7	39-7	407	41-7	42-7
		_													
EMORRHAGE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
RTICOLLIS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ó
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ő
RREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	Ō	Ō	Õ	õ	õ	õ	õ
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Ő	Õ	Ő	õ
	3000 ppm	0	0	0	0	Ő	Õ	Ő	õ	Ő	Ő	Ő	0	0	Ő
BNORMAL RESPIRATION	Contral	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	Ō	Ő	0	õ	Õ	Ő	õ	Ö	Ő
	1500 ppm	Ő	õ	õ	Ő	Ő	Ő	õ	õ	0	0	0	0	0	0
	3000 ppm	Ő	õ	õ	õ	õ	0 0	0	ŏ	0	0	0	0	0	0
BNORMAL RESPIRA.SOUND	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ő	õ	0	ŏ	Õ	õ	Ő	0	0	õ	0	0	0	0
	1500 ppm	õ	Ő	õ	Õ	Ő	ŏ	õ	ŏ	Ő	õ	Ő	0	0	0
	3000 ppm	Ő	Ő	0 0	0	Ő	Ő	0	0	0	0	0	0	0	0
EMATURIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Ő	Ö	0 0	Õ	0	0	0	0	0	0	0	0	0	0
	1500 ppm	Ő	Ő	0	Ő	0	0	0	0	0	0	0			-
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0 0	0 0	0 0
ED URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	^
	750 ppm	0	õ	0	ŏ	0	0	0	0	0	0		-	•	0
	1500 ppm	0 0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		v	v	v	v	v	v	v	v	v	v	U	v	U	0
ELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS  $\sim$ 

SEX : FEMALE

STUDY NO. : 0267

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

Clinical sign	Group Name	Admini	stration W	eek-day					**						
		43-7	44-7	45-7	46-7	47-7	48-7	49-7	50-7	51-7	52-7	53-7	54-7	55-7	56-7
EMORRHAGE	Contral	0	0	0	0	0	0	0	0	0	0	0	0	. 0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ORTICOLLIS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0 -	0	0	0	0	0	0	0	0	Ő	Ő	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
RREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	Ō	Ō	Õ	õ	õ	Õ	ŏ	õ	ů 0	Ő	· 0	0	0
	1500 ppm	0	0	Ō	0	Õ	Õ	0	õ	ŏ	Õ	0 0	õ	Ő	0
	3000 maa	0	0	0	0	Ō	0	õ	õ	Ő	õ	ŏ	õ	ő	0
BNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	ŏ	0	Ő	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	Ő	0	0 0	0	0	0.	0	0	0	0	0	0	-	0
	3000 ppm	0 0	0	õ	0	0	0	0	0	0	0	0	0	0 0	0
BNORMAL RESPIRA.SOUND	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
IDROMINE NEDI TRA. DOOND	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	•	0
	1500 ppm	0	0	0	0	0	0	-	0	•	-	-	•	0	0
	3000 ppm	ŏ	0	0	0	0	0	0	0	0 0	0 0	0 0	0	0	0
IEMATURIA	Cantan	0	0	٥	0	0	•	•	<u>^</u>	<u>^</u>		<u>,</u>			
LUNIONIA	Control 750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm 1500 ppm	0	0	0	0	0	0	-	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	SUUV PPM	v	v	U	v	U	0	0	0	0	0	0	0	0	0
ED URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ő	Õ
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ō	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ô

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS ~\_\_\_\_

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SEX : FEMALE

linical sign	Group Name	Admin	istration W	eek-dav											
		57-7	58-7	59-7	60-7	61-7	627	63-7	647	65-7	66-7	67-7	68-7	69-7	70-7
	······································											····#			
EMORRHAGE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Ô	Ő	Ő
	1500 ppm	0	0	Ō	1	1	0	0	0	Õ	0	õ	0	õ	1
	3000 ppm	0	0	Ő	ō	1	Ő	õ	õ	0	Ő	Ő	0	0	0
ORTICOLLIS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	. 0
	750 ppm	õ	Ő	Ő	Ő	õ	õ	õ	õ	Ő	0	0	0	0	0
	1500 ppm	Ő	Ő	0	0 0	0	0	ŏ	0	0	0	0	0	0	
	3000 ppm	õ	0	0	0	0	0	0	0	0	0	0	0	0	0 0
RREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	^
ALGOLIAN DALATITING	750 ppm	0	0	0	0	0	0		-		-	0	0	0	0
	1500 ppm 1500 ppm	0	0	0		-		0	0	0	0	0	0	0	0
				-	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
BNORMAL RESPIRA.SOUND	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ō
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EMATURIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ó
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Õ	0	0	Ő
	3000 ppm	0	0	0	0	0	0	0	0	õ	õ	õ	õ	0 0	0
ED URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	Ō	Ő	Ő	õ	Ő	ů	õ	Õ	0	0	Ő
	1500 ppm	0	Ő	Ő	ů	õ	ŏ	õ	Ö	ŏ	Ő	0	0	0	0
	3000 ppm	ő	0 0	Ő	Ő	õ	õ	0	ŏ	0	0	0	0	0	0
ELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	Õ	õ	õ	ŏ	õ	ŏ	õ	õ	Õ	Ň	0	0	0	0
	1500 ppm	Ö	ŏ	0 0	ŏ	0	Ő	0	ŏ	0	0	0	0	0	•
	3000 ppm	0	Ő	0	Ő	Ö	. 0	0	0	0	0	0	0	0	0
		v	v	v	v	v	v	v	v	v	v	v	v	v	0

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS · \_ ·

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SEX : FEMALE

Clinical sign	Group Name	Admini	stration W	eek-day											
		71-7	72-7	73-7	74-7	75-7	76-7	77-7	78 <del>-</del> 7	79–7	80-7	81-7	82-7	837	84-7
EMORRHAGE	Control	0	0	0	0	0	0	0	0	0	0	1	2	1	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	1	0	0	0	1	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	1	0	0	0	0	0	1	0
DRTICOLLIS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	1	1	1	1	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	Ō	0	0	0
RREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	Ō	Ō	Õ	Ő
	3000 ppm	0	0	0	0	0	0	0	Ō	Ō	õ	Õ	õ	Ő	Ő
BNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ó
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
BNORMAL RESPIRA.SOUND	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
IEMATURIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	Ó	0	0	Ō	0	0	Ő	ŏ
	3000 ppm	0	0	0	0	0	0	0	0	Ō	õ	0	Ő	õ	Ő
ED URINE	Control	0	0	0	0	0	0	0	0	. 0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ō	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	Ō	õ	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	Ő	0	0
ELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Ō	Ō	1
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ó	Ő

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : FEMALE

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Clinical sign	Group Name	Admini	stration W	eek-day											
<u></u>		85-7	86-7	87-7	88-7	89-7	90-7	91-7	92-7	93-7	94-7	95-7	96-7	97-7	98-7
IEMORRHAGE	Control	0	0	0	0	0	0	0	0	0	0	2	1	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	1	0	0	1
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	ō
ORTICOLLIS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	Ő	õ	õ
	3000 ppm	0	0	0	0	0	0	0	0	0	õ	õ	õ	õ	Ő
RREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	Ō	Ő	ő	õ
	1500 ppm	0	0	0	0	0	0	0	0	Ō	0	Ō	Ő	ů	ŏ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	Ő	Ő	õ	1
BNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	Ō	Ő	õ	ŏ
	1500 ppm	0	0	0	0	0	Ó	0	0	Õ	0	Õ	õ	õ	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	õ	õ	õ	õ	1
BNORMAL RESPIRA.SOUND	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	Ó	0	0	Ő
	1500 ppm	0	0	0	0	0	0	0	0	Ō	0	Õ	Ő	õ	ŏ
	3000 ppm	0	0	0	0	0	0	0	0	0	0	Õ	Ő	1	1
IEMATURIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	Õ	Ő	õ	õ	õ	0
	1500 ppm	0	0	0	0	0	0	Ō	0	0	Õ	õ	Ő	0	Ő
	3000 ppm	0	0	0	0	õ	õ	Ő	õ	ő	õ	1	0	0	0
RED URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	Ō	Ō	Ō	Õ	õ	0	õ	0	Ő	0	0	0
	1500 ppm	0	ō	õ	õ	õ	õ	0	0	õ	0	0	0	0	0
	3000 ppm	0	0	Õ	õ	Ő	õ	0	0	0	0	0	0	0	0
ELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	1	Õ	ů	Ő	Ő	õ	0	0	0	0	0	0	0	0
	1500 ppm	Ô	õ	Õ	õ	õ	0	0	0	0	0	0	0	0	0
	3000 ppm	ů	õ	õ	õ	õ	0	0	Ő	0	Ö	0	0		
		v	v	0	v	v	v	v	v	v	v	U	v	0	0

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS ~~

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## SEX : FEMALE

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Clinical sign	Group Name	Admin	istration [	leek-day		-			·····
-		99-7	100-7	101-7	102-7	103-7	104-7		
								·	
HEMORRHAGE	Contract	•		•	•	•			
ACHOARAAGE	Control	0	1	0	0	0	0		
	750 ppm 1500 ppm	0		0	0	0	0		
			1	1	1	0	1		
	3000 ppm	0	U	0	0	0	0		
TORTICOLLIS	Control	0	0	0	0	0	0		
	750 ppm	õ	0	0	0	0	0		
	1500 ppm	0	0	0	0				
	3000 ppm	0	0	0	0	0	0		
		v	v	v	v	0	0		
IRREGULAR BREATHING	Control	0	0	0	1	0	0		
timesoum breathing	750 ppm	0	0	0	0	0	0		
	1500 ppm	0	0	0	0	0	0		
	3000 ppm	0	0	0	0	0	0		
		v	v	U	v	v	v		
ABNORMAL RESPIRATION	Control	0	0	0	1	0	0		
	750 ppm	0	0	0	0	Ő	õ		
	1500 ppm	0	0	Ō	Ő	ŏ	õ		
	3000 ppm	Ō	Ō	Ő	Õ	ŏ	õ		
	•••		-		•	•	·		
ABNORMAL RESPIRA.SOUND	Control	0	0	0	0	0	0		
	750 ppm	0	0	0	0	0	0		
	1500 ppm	0	0	0	0	0	0		
	3000 ppm	0	0	0	0	0	0		
HEMATURIA	Control	0	0	0	0	0	0		
	750 ppm	0	0	0	0	0	0		
	1500 ppm	0	0	0	0	0	0		
	3000 ppm	0	3	2	5	0	0		
RED URINE	Control	0	0	0	0	0	0		
	750 ppm	0	0	0	0	0	0		
	1500 ppm	0	0	0	0	0	0		
	3000 ppm	0	0	0	0	5	9		
	<b>.</b>		_						
YELLOW URINE	Contral	0	0	0	0	0	0		
	750 ppm	0	0	0	0	0	0		
	1500 ppm	0	0	0	0	0	0		
	3000 ppm	U	0	0	0	0	0		

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : FEMALE

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linical sign	Group Name	Admini	stration We	ek-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	14-7
0005 07002		_													
OOSE STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
MALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	Ô	Ô	Ő
	3000 ppm	0	0	0	0	0	0	0	0	0	0	õ	Ö	õ	Ő
LIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	٥
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	Ő	Ő	õ
	1500 ppm	0	0	0	0	0	0	Ō	Ō	0	Ō	õ	Ő	0	õ
	3000 ppm	0	0	0	0	0	0	0	Ō	Ō	Ô	õ	õ	õ	ŏ
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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : FEMALE

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Clinical sign	Group Name	Admini	stration W	leek-day											·
		15–7	16-7	17-7	18-7	197	20-7	21–7	22–7	23-7	24-7	257	26-7	27-7	28-7
LOOSE STOOL	Control	0	0	0	0	0	0	0	٥	0	•	0	•	0	<u>^</u>
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		v	v	v	v	v	v	v	v	v	v	U	v	0	V
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	Ō	0	0	0	0	Ő	Ő	0 0	õ
	1500 ppm	0	0	0	0	0	0	0	Ó	0	0	0	0	Õ	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DLIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Ō
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : FEMALE

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Clinical sign	Group Name	Admini	istration W	eek-day											
		29–7	307	31-7	32-7	33-7	34-7	35-7	36-7	37-7	38-7	39-7	40-7	41-7	42-7
OOSE STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
MALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
LIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	750 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Admini | stration W | eek-day |      |         |     |      | ***** |      | • •   |      |      |      |        |
|---------------|------------|--------|------------|---------|------|---------|-----|------|-------|------|-------|------|------|------|--------|
|               |            | 43-7   | 44–7       | 45-7    | 46-7 | 47-7    | 487 | 49-7 | 50-7  | 51-7 | 52-7  | 53-7 | 54-7 | 55-7 | 56-7   |
| 0000 0000     |            |        |            |         |      |         |     |      |       |      |       |      |      |      |        |
| LOOSE STOOL   | Control    | 0      | 0          | 0       | 0    | 0       | 0   | 0    | 0     | 0    | 0     | 0    | 0    | 0    | 0      |
|               | 750 ppm    | 0      | 0          | 0       | 0    | 0       | 0   | 0    | 0     | 0    | 0     | 0    | 0    | 0    | 0      |
|               | 1500 ppm   | 0      | 0          | 0       | 0    | 0       | 0   | 0    | 0     | 0    | 0     | 0    | 0    | 0    | 0      |
|               | 3000 ppm   | 0      | 0          | 0       | 0    | 0       | 0   | 0    | 0     | 0    | 0     | 0    | 0    | 0    | 0      |
| MALL STOOL    | Control    | 0      | 0          | 0       | 0    | 0       | 0   | 0    | 0     | 0    | 0     | 0    | 0    | 0    | 0      |
|               | 750 ppm    | 0      | 0          | 0       | 0    | 0       | 0   | 0    | 0     | 0    | 0     | 0    | 0    | 0    | 0      |
|               | 1500 ppm   | 0      | 0          | 0       | 0    | 0       | 0   | 0    | 0     | 0    | 0     | 0    | 0    | 0    | Ő      |
|               | 3000 ppm   | 0      | 0          | 0       | 0    | 0       | 0   | 0    | 0     | 0    | 0     | 0    | 0    | 0    | 0      |
| LIGO-STOOL    | Control    | 0      | 0          | 0       | 0    | 0       | 0   | 0    | 0     | 0    | 0     | 0    | 0    | . 0  | 0      |
|               | 750 ppm    | 0      | 0          | 0       | 0    | 0       | 0   | 0    | 0     | 0    | 0     | 0    | 0    | õ    | Ő      |
|               | 1500 ppm   | 0      | 0          | 0       | 0    | 0       | 0   | 0    | 0     | 0    | Ő     | 0    | 0    | 0    | õ      |
|               | 3000 ppm   | 0      | 0          | 0       | 0    | 0       | Ó   | 0    | Ō     | 0    | 0     | 0    | õ    | 0    | ů<br>0 |
|               |            | •      |            |         |      |         | ·   | ·    | Ū     | · ·  | Ŭ     | Ū    | Ū    | Ũ    | Ū      |
| (HAN190)      |            |        |            |         |      | <b></b> |     |      |       |      | ····· |      |      |      |        |

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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## SEX : FEMALE

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| Clinical sign | Group Name | Admini | stration W | eek-day |      |      |      |      |      |      |      |         |          |          |          |
|---------------|------------|--------|------------|---------|------|------|------|------|------|------|------|---------|----------|----------|----------|
|               |            | 57-7   | 58-7       | 59-7    | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7    | 68–7     | 69-7     | 70-7     |
| OOSE STOOL    | Control    | 0      | 0          | 0       | 0    | ٥    | ٥    | ^    | ^    | ^    | ٥    | 0       | <u>^</u> | <u>^</u> | <u>^</u> |
| NODE STOLE    | 750 ppm    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       | 0        | 0        | 0        |
|               | 1500 ppm   | 0      | 0          | 0       | 0    | 0    |      | -    | 0    | 0    | 0    | 0       | 0        | 0        | 0        |
|               |            | 0      | 0          | 0       | 0    |      | 0    | 0    | 0    | 0    | 0    | 0       | U        | 0        | 0        |
|               | 3000 ppm   | U      | U          | U       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       | 0        | 0        | 0        |
| MALL STOOL    | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       | 0        | 0        | 0        |
|               | 750 ppm    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       | 0        | 0        | 0        |
|               | 1500 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       | 0        | 0        | 0        |
|               | 3000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       | 0        | 0        | 1        |
| LIGO-STOOL    | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       | 0        | 0        | 0        |
|               | 750 ppm    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       | 0        | 0        | 0        |
|               | 1500 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       | 0        | 0        | 0        |
|               | 3000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       | 0        | 0        | 0        |
|               |            |        |            |         |      |      |      |      | -    | -    | ·    | ·       | Ū        | ·        |          |
| (HAN190)      |            |        |            |         |      |      |      | 9,11 |      |      |      | ******* |          |          |          |

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : FENALE

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| Clinical sign | Group Name | Admini | stration W | eek-day |      |         |      |      |     |      |      |      |        |      | ·    |
|---------------|------------|--------|------------|---------|------|---------|------|------|-----|------|------|------|--------|------|------|
| ·····         |            | 71-7   | 72-7       | 73-7    | 74-7 | 75-7    | 76-7 | 77-7 | 787 | 79-7 | 80-7 | 81-7 | 82-7   | 83-7 | 84-7 |
| 000E 07001    |            |        |            |         |      |         | -    |      |     |      |      |      |        |      |      |
| LOOSE STOOL   | Contral    | 0      | 0          | 0       | 0    | 0       | 0    | 0    | 0   | 0    | 0    | 0    | 0      | 0    | 0    |
|               | 750 ppm    | 0      | 0          | 0       | 0    | 0       | 0    | 0    | 0   | 0    | 0    | 0    | 0      | 0    | Ó    |
|               | 1500 ppm   | 0      | 0          | 0       | 0    | 0       | 0    | 0    | 0   | 0    | 0    | 0    | 0      | 0    | 0    |
|               | 3000 ppm   | 0      | 0          | 0       | 0    | 0       | 0    | 0    | 0   | 0    | 0    | 0    | 0      | 0    | 0    |
| MALL STOOL    | Control    | 0      | 0          | 0       | 0    | 0       | 0    | 0    | 0   | 0    | 0    | 0    | 0      | 0    | 0    |
|               | 750 ppm    | 0      | 0          | 0       | 0    | 0       | 0    | 0    | 1   | 1    | 1    | õ    | õ      | Õ    | 0    |
|               | 1500 ppm   | 0      | 0          | 0       | 0    | 0       | Ō    | 0    | 0   | ō    | 0    | Õ    | ő      | 0    | 0    |
|               | 3000 ppm   | 0      | 0          | 0       | 0    | 1       | 0    | 0    | 0   | Ő    | õ    | ő    | ő      | Ő    | 1    |
| LIGO-STOOL    | Control    | 0      | 0          | 0       | 0    | 0       | 0    | 0    | 0   | 0    | 0    | 0    | ٥      | 0    | 0    |
|               | 750 ppm    | 0      | 0          | 0       | 0    | 0       | Ó    | 1    | 1   | 1    | ĩ    | õ    | õ      | õ    | 1    |
|               | 1500 ppm   | 0      | 0          | 0       | 0    | 0       | Ō    | ō    | ō   | ō    | 0    | õ    | Ő      | õ    | 0    |
|               | 3000 ppm   | 0      | 0          | 0       | 1    | 1       | õ    | 0    | ŏ   | Ő    | õ    | Ő    | 0<br>0 | 0    | 1    |
|               |            |        |            |         | -    | -       | •    | v    | v   | Ū    | Ū    | Ū    | v      | U    | 1    |
| (HAN190)      |            |        |            |         |      | <b></b> |      |      |     |      |      |      |        |      |      |

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BAIS 3

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS ·\_\_\_·

SEX : FEMALE

PAGE: 95

| Clinical sign | Group Name | Admini | stration W | eek-day |      |      |      |      |      |      |      |      |      |      |      |
|---------------|------------|--------|------------|---------|------|------|------|------|------|------|------|------|------|------|------|
|               |            | 85-7   | 86-7       | 87–7    | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
|               |            |        |            |         |      |      |      |      |      |      |      |      |      |      |      |
| LOOSE STOOL   | Contral    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 750 ppm    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 1500 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 3000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| MALL STOOL    | Control    | 0      | 0          | 0       | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 1    | 0    | 0    | 1    |
|               | 750 ppm    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 2    |
|               | 1500 ppm   | 0      | 0          | 0       | 0    | 0    | Ó    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 3000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 2    | 2    |
| )LIG0-STOOL   | Control    | 0      | 0          | 0       | 0    | 0    | 1    | 1    | 0    | 0    | . 0  | 1    | 0    | 1    | 1    |
|               | 750 ppm    | 1      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 2    | 2    | 1    |
|               | 1500 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | Ō    | 0    | 1    | 0    |
|               | 3000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | Ō    | 1    | 1    | 1    |
|               |            |        |            |         |      |      |      |      |      |      |      |      | -    | -    | -    |
| (HAN190)      |            |        |            |         |      |      |      |      |      |      |      |      |      |      |      |

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : FEMALE

PAGE: 96

| Clinical sign | Group Name | Admin | istration | leek-day |       |       |          |
|---------------|------------|-------|-----------|----------|-------|-------|----------|
|               |            | 997   | 100-7     | 101-7    | 102-7 | 103-7 | 104-7    |
|               |            |       |           |          |       |       |          |
| LOOSE STOOL   | Control    | 0     | 0         | 0        | 0     | 1     | 0        |
|               | 750 ppm    | 0     | 0         | 0        | 0     | ō     | Õ        |
|               | 1500 ppm   | 0     | 0         | 0 ·      | 0     | 0     | 0        |
|               | 3000 ppm   | 0     | 0         | 0        | 0     | 0     | 0        |
| SMALL STOOL   | Control    | 0     | 0         | T        | 0     | 0     | <u>^</u> |
|               | 750 ppm    | 2     | 1         | 2        | 3     | 3     | 2        |
|               | 1500 ppm   | 1     | 1         | 2        | 2     | 1     | 2        |
|               | 3000 ppm   | 1     | 1         | 0        | 0     | 0     | 0        |
|               |            | 1     | Ŧ         | v        | 0     | 0     | 0        |
| OLIGO-STOOL   | Control    | 2     | 1         | 1        | 3     | 2     | 1        |
|               | 750 ppm    | 1     | 1         | 2        | 2     | 1     | 2        |
|               | 1500 ppm   | 1     | 1         | 0        | ō     | Ō     | 0        |
|               | 3000 ppm   | 0     | 0         | 0        | 0     | Ō     | 1        |

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(HAN190)

BAIS 3

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, RAT : MALE

(2-YEAR STUDY)

| up Name  | Admini | stration | week |     |      |     |      |      |          |      |      |      |          |      |  |
|----------|--------|----------|------|-----|------|-----|------|------|----------|------|------|------|----------|------|--|
|          | 0      |          | 1    |     | 2    |     | 3    |      | 4        |      | 5    |      | 6        |      |  |
| Control  | 123±   | 4        | 152± | 6   | 180± | 9   | 203± | 11   | $222\pm$ | 13   | 238± | 16   | $251\pm$ | 18   |  |
| 750 ppm  | 123±   | 4        | 150± | 6   | 176± | 9*  | 196± | 11** | $212\pm$ | 14** | 226± | 16** | 240±     | 18** |  |
| 1500 ppm | 123±   | 4        | 145± | 6** | 170± | 8** | 190± | 11** | 207±     | 14** | 223± | 16** | 236±     | 18** |  |
| 3000 ppm | 123±   | 4        | 136± | 6** | 158± | 8** | 176± | 9**  | 190±     | 11** | 204± | 14** | 216±     | 16** |  |

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| p Name   | Admin | istration | week     |      |      |      |          |      |          |      |      |      |          |      |
|----------|-------|-----------|----------|------|------|------|----------|------|----------|------|------|------|----------|------|
|          | 7     |           | 8        |      | 9    |      | 10       |      | 11       |      | 12   |      | 13       |      |
| Control  | 263±  | 21        | 272±     | 22   | 282± | 23   | 292±     | 24   | 300±     | 25   | 307± | 26   | $316\pm$ | 26   |
| 750 ppm  | 252±  | 19**      | 262±     | 20*  | 272± | 21*  | 281±     | 21*  | $290\pm$ | 22   | 296± | 22   | 306±     | 22   |
| 1500 ppm | 248±  | 19**      | 259±     | 20** | 269± | 21** | 278±     | 22** | 287±     | 21*  | 292± | 21*  | 302±     | 21   |
| 3000 maa | 226土  | 17**      | $235\pm$ | 17** | 245± | 18** | $252\pm$ | 18** | 259±     | 18** | 263± | 17** | 272±     | 17** |

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| TUDY NO.: 0267<br>NIMAL : RAT F344/DuCrj<br>NIT : g<br>EPORT TYPE : A1 104<br>EX : MALE |          |           |          |      | BODY WEIGHT<br>ALL ANIMALS | CHANGES | (SUMMARY) |        |      |      |      |      |          | PAGE | : 3    |  |
|-----------------------------------------------------------------------------------------|----------|-----------|----------|------|----------------------------|---------|-----------|--------|------|------|------|------|----------|------|--------|--|
| Group Name                                                                              | Admin    | istration |          |      | ·····                      |         |           |        |      |      |      |      |          |      |        |  |
|                                                                                         | 14       |           | 18       |      | 22                         |         | 26        |        | 30   |      | 34   |      | 38       |      |        |  |
| Control                                                                                 | 320±     | 26        | 339±     | 24   | $361\pm$                   | 24      | 379±      | 24     | 394± | 25   | 407± | 25   | 419±     | 24   |        |  |
| 750 mag                                                                                 | $310\pm$ | 22        | 330±     | 21   | 351±                       | 20      | 369±      | 21     | 385± | 21   | 398± | 21   | 410±     | 21   |        |  |
| 1500 ppm                                                                                | 306±     | 21**      | $325\pm$ | 20** | 344±                       | 21**    | 359±      | 22**   | 373± | 21** | 385± | 20** | $395\pm$ | 21** |        |  |
| mag 0008                                                                                | 276±     | 18**      | 293±     | 19** | 309±                       | 20**    | 323±      | 21**   | 333± | 22** | 343± | 22** | $352\pm$ | 23** |        |  |
|                                                                                         |          |           |          |      | ····                       |         |           |        |      |      |      |      |          |      |        |  |
| Significant difference ;                                                                | *:P≦     | 0.05      | **:P≦0.0 | 01   |                            |         | Test of D | unnett |      |      |      |      |          |      |        |  |
| HAN260)                                                                                 |          |           |          |      |                            | *****   |           |        |      |      |      |      |          |      | BAIS 3 |  |

| STUDY NO. : 0267<br>ANIMAL : RAT F344/D_Crj<br>UNIT : g<br>REPORT TYPE : A1 104 |      |          |             |      | BODY WEIGHT<br>ALL ANIMALS | CHANGES | (SUMMARY) |           |      |         |          |      |          |      |         |
|---------------------------------------------------------------------------------|------|----------|-------------|------|----------------------------|---------|-----------|-----------|------|---------|----------|------|----------|------|---------|
| SEX : MALE                                                                      |      |          |             |      |                            |         |           |           |      |         |          |      |          |      | PAGE: 4 |
| Group Name                                                                      |      | istratio | n week      |      |                            |         |           |           |      |         |          |      |          | ·    |         |
|                                                                                 | 42   |          | 46          |      | 50                         |         | 54        |           | 58   |         | 62       |      | 66       |      |         |
| Control                                                                         | 430± | 26       | 440±        | 26   | 449±                       | 26      | 454±      | 25        | 462± | 27      | 469±     | 28   | 475±     | 28   |         |
| 750 ppm                                                                         | 421± | 23       | 432±        | 23   | 440±                       | 22      | 447±      | 20        | 453± | 22      | $461\pm$ | 23   | 466±     | 23   |         |
| 1500 ppm                                                                        | 405± | 23**     | 415±        | 23** | 422±                       | 23**    | 428±      | 22**      | 432± | 23**    | 440±     | 23** | 445±     | 24** |         |
| 3000 ppm                                                                        | 361± | 24**     | 367±        | 24** | 372±                       | 24**    | 378±      | 24**      | 381± | 24**    | 384±     | 24** | $387\pm$ | 25** |         |
| Significant difference ;                                                        | *:P≦ | 0.05     | ** : P ≦ 0. | 01   |                            |         | Test of D | nnett     |      |         |          |      |          |      |         |
| (HAN260)                                                                        |      |          |             |      |                            |         |           | · ··· ··· |      | <u></u> |          |      |          |      | BAIS 3  |

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|              |                                    |                                                                      |                                                                                                 | BODY WEIGHT<br>ALL ANIMALS                                                                                                        | CHANGES                                                                                                                                                                                                                                       | (SUMMARY)                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | PAGE : 5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|--------------|------------------------------------|----------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Admini<br>70 | istration                          | wəək<br>74                                                           |                                                                                                 | 78                                                                                                                                |                                                                                                                                                                                                                                               | 82                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                | 86                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                | 90                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                | 94                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | · · · · · · · · · · · · · · · · · · ·                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| 479±         | 28                                 | 481±                                                                 | 33                                                                                              | 487±                                                                                                                              | 29                                                                                                                                                                                                                                            | 489±                                                                                                                                                                                                                                                                  | 30                                                                                                                                                                                                                                                                             | 481±                                                                                                                                                                                                                                                                                           | 40                                                                                                                                                                                                                                                                                                                                                                                             | 481±                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 35                                                                                                                                                                                                                                                                                                                                                                             | 474±                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 45                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| 469±         | 22                                 | 474±                                                                 | 24                                                                                              | 478±                                                                                                                              | 25                                                                                                                                                                                                                                            | 479±                                                                                                                                                                                                                                                                  | 26                                                                                                                                                                                                                                                                             | 479±                                                                                                                                                                                                                                                                                           | 26                                                                                                                                                                                                                                                                                                                                                                                             | 473±                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 29                                                                                                                                                                                                                                                                                                                                                                             | 472±                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 31                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| 444±         | 22**                               | 445±                                                                 | 23**                                                                                            | 446±                                                                                                                              | 24**                                                                                                                                                                                                                                          | 444±                                                                                                                                                                                                                                                                  | 35**                                                                                                                                                                                                                                                                           | 446±                                                                                                                                                                                                                                                                                           | 22**                                                                                                                                                                                                                                                                                                                                                                                           | 446±                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 23**                                                                                                                                                                                                                                                                                                                                                                           | 443±                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 33**                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| 387±         | 24**                               | 387±                                                                 | 27**                                                                                            | 387±                                                                                                                              | 30**                                                                                                                                                                                                                                          | 383±                                                                                                                                                                                                                                                                  | 33**                                                                                                                                                                                                                                                                           | 383±                                                                                                                                                                                                                                                                                           | 25**                                                                                                                                                                                                                                                                                                                                                                                           | 381±                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 26**                                                                                                                                                                                                                                                                                                                                                                           | 375±                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 28**                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| *:P≦         | 0.05                               | ** : P ≦ 0.1                                                         | 01                                                                                              |                                                                                                                                   |                                                                                                                                                                                                                                               | Test of D                                                                                                                                                                                                                                                             | Innett                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                | <del></del>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| -            | 70<br>479±<br>469±<br>444±<br>387± | $70$ $479 \pm$ $28$ $469 \pm$ $22$ $444 \pm$ $22**$ $387 \pm$ $24**$ | $479\pm$ $28$ $481\pm$ $469\pm$ $22$ $474\pm$ $444\pm$ $22**$ $445\pm$ $387\pm$ $24**$ $387\pm$ | $70$ $74$ $479\pm$ $28$ $481\pm$ $33$ $469\pm$ $22$ $474\pm$ $24$ $444\pm$ $22**$ $445\pm$ $23**$ $387\pm$ $24**$ $387\pm$ $27**$ | ALL ANIMALS         Administration       week       74       78 $70$ $74$ $78$ 78 $479\pm$ $28$ $481\pm$ $33$ $487\pm$ $469\pm$ $22$ $474\pm$ $24$ $478\pm$ $444\pm$ $22**$ $445\pm$ $23**$ $446\pm$ $387\pm$ $24**$ $387\pm$ $27**$ $387\pm$ | ALL ANIMALS         Administration       week       74       78 $70$ $74$ $78$ 78 $479\pm$ $28$ $481\pm$ $33$ $487\pm$ $29$ $469\pm$ $22$ $474\pm$ $24$ $478\pm$ $25$ $444\pm$ $22**$ $445\pm$ $23**$ $446\pm$ $24**$ $387\pm$ $24**$ $387\pm$ $27**$ $387\pm$ $30**$ | ALL ANIMALS         Administration       week       74       78       82 $479\pm$ 28 $481\pm$ 33 $487\pm$ 29 $489\pm$ $469\pm$ 22 $474\pm$ 24 $478\pm$ 25 $479\pm$ $444\pm$ 22** $445\pm$ 23** $446\pm$ 24** $444\pm$ $387\pm$ $24**$ $387\pm$ $27**$ $387\pm$ $30**$ $383\pm$ | ALL ANIMALS         Administration       week       74       78       82 $479\pm$ 28 $481\pm$ 33 $487\pm$ 29 $489\pm$ 30 $469\pm$ 22 $474\pm$ 24 $478\pm$ 25 $479\pm$ 26 $444\pm$ 22** $445\pm$ 23** $446\pm$ 24** $444\pm$ 35** $387\pm$ 24** $387\pm$ $27**$ $387\pm$ $30**$ $383\pm$ $33**$ | ALL ANIMALS         Administration       week       74       78       82       86 $70$ $74$ $78$ $82$ $86$ $479\pm$ $28$ $481\pm$ $33$ $487\pm$ $29$ $489\pm$ $30$ $481\pm$ $469\pm$ $22$ $474\pm$ $24$ $478\pm$ $25$ $479\pm$ $26$ $479\pm$ $444\pm$ $22**$ $445\pm$ $23**$ $446\pm$ $24**$ $444\pm$ $35**$ $446\pm$ $387\pm$ $24**$ $387\pm$ $27**$ $387\pm$ $30**$ $383\pm$ $33**$ $383\pm$ | ALL ANIMALS         Administration       week       74       78       82       86 $479 \pm$ 28       481 \pm       33       487 \pm       29       489 \pm       30       481 \pm       40 $469 \pm$ 22       474 \pm       24       478 \pm       25       479 \pm       26       479 \pm       26 $444 \pm$ 22**       445 \pm       23**       446 \pm       24**       444 ±       35**       446 ±       22**         387 ±       24**       387 ±       27**       387 ±       30**       383 ±       33**       383 ±       25** | ALL ANIMALS         Administration       week       74       78       82       86       90 $479\pm$ 28 $481\pm$ 33 $487\pm$ 29 $489\pm$ 30 $481\pm$ 40 $481\pm$ $469\pm$ 22 $474\pm$ 24 $478\pm$ 25 $479\pm$ 26 $473\pm$ $444\pm$ 22** $445\pm$ 23** $446\pm$ 24** $444\pm$ 35** $446\pm$ 22** $446\pm$ $387\pm$ 24** $387\pm$ $30**$ $383\pm$ $33**$ $383\pm$ $25**$ $381\pm$ | ALL ANIMALS         Administration       week       74       78       82       86       90         479±       28       481±       33       487±       29       489±       30       481±       40       481±       35         469±       22       474±       24       478±       25       479±       26       473±       29         444±       22**       445±       23**       446±       24**       444±       35**       446±       22**       446±       23**         387±       24**       387±       27**       387±       30**       383±       33**       383±       25**       381±       26** | Administration       week       74       78       82       86       90       94         479±       28       481±       33       487±       29       489±       30       481±       40       481±       35       474±         469±       22       474±       24       478±       25       479±       26       473±       29       472±         444±       22**       445±       23**       446±       24**       444±       35**       446±       22**       446±       23**       443±         387±       24**       387±       27**       387±       30**       383±       33**       383±       25**       381±       26**       375± |

| STUDY NO.: 0267<br>ANIMAL : RAT F344/DuCrj<br>UNIT : g |       |          |             |      | BODY WEIGHT<br>ALL ANIMALS | CHANGES | (SUMMARY)       |          |
|--------------------------------------------------------|-------|----------|-------------|------|----------------------------|---------|-----------------|----------|
| REPORT TYPE : A1 104<br>SEX : MALE                     |       |          |             |      |                            |         |                 | PAGE : 6 |
| Group Name                                             |       | istratio |             |      |                            |         |                 |          |
|                                                        | 98    |          | 102         |      | 104                        |         |                 |          |
|                                                        |       |          |             |      |                            |         |                 |          |
| Control                                                | 470±  | 40       | 457±        | 37   | $452\pm$                   | 41      |                 |          |
| 750                                                    | 405 1 | 00       | 150 1       | 10   |                            |         |                 |          |
| 750 ppm                                                | 465±  | 39       | 458±        | 46   | 454±                       | 38      |                 |          |
| 1500 ppm                                               | 440±  | 44**     | 432±        | 22*  | $425\pm$                   | 22*     |                 |          |
|                                                        |       |          |             |      |                            |         |                 |          |
| 3000 ppm                                               | 368±  | 29**     | 360±        | 31** | 353±                       | 31**    |                 |          |
|                                                        |       |          |             |      |                            |         |                 |          |
|                                                        |       |          | t           |      | 1V.1X.J                    |         |                 |          |
| Significant difference ;                               | *:P≦  | 0.05     | ** : P ≦ 0. | 01   |                            |         | Test of Dunnett |          |
| (HAN260)                                               |       |          |             |      |                            |         |                 | BAIS 3   |

APPENDIX B 2

### BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

(2-YEAR STUDY)

| Name          | Admin | stration | week |     |      |     |      |     |          |     |          |     |          |     |
|---------------|-------|----------|------|-----|------|-----|------|-----|----------|-----|----------|-----|----------|-----|
|               | 0     |          | 1    |     | 2    |     | 3    |     | 4        |     | 5        |     | 6        |     |
| Control       | 100±  | 3        | 116± | 4   | 130± | 5   | 139± | 6   | $147\pm$ | 7   | 153±     | 8   | $157\pm$ | 8   |
| 750 ppm       | 100±  | 3        | 115± | 5   | 128± | 6   | 136± | 7   | 145±     | 7   | $151\pm$ | 9   | 154±     | 9   |
| 1500 ppm      | 100±  | 3        | 113± | 4** | 125± | 5** | 133± | 6** | $141\pm$ | 7** | $146\pm$ | 8** | 150±     | 9** |
| 3000 mag 0008 | 100±  | 3        | 106± | 4** | 119± | 5** | 126± | 6** | 133±     | 8** | 139±     | 8** | 143±     | 9** |

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| Name          | Admin    | istration | week     |      |          |      |          |      |   |          |      |      |      | • • • • • • • • • • • • • • • • • • • |      |
|---------------|----------|-----------|----------|------|----------|------|----------|------|---|----------|------|------|------|---------------------------------------|------|
|               | 7        |           | 8        |      | 9        |      | 10       |      |   | 11       |      | 12   |      | 13                                    |      |
| Control       | 161±     | 8         | 163±     | 8    | $167\pm$ | 9    | $172\pm$ | 10   |   | 174±     | 10   | 176± | 10   | 179±                                  | 10   |
| 750 ppm       | 159±     | 10        | $161\pm$ | 10   | 165±     | 10   | 169±     | 11   | × | $172\pm$ | 10   | 173± | 11   | 177±                                  | 10   |
| 1500 pom      | $155\pm$ | 9**       | $156\pm$ | 10** | 160±     | 11** | 164±     | 11** |   | 166±     | 11** | 168± | 12** | 171±                                  | 11** |
| 3000 mag 0008 | 147±     | 9**       | 149±     | 9**  | 152±     | 9**  | 156±     | 9**  |   | 159±     | 9**  | 160± | 9**  | 163±                                  | 9**  |

| FUDY NO. : 0267<br>NIMAL : RAT F344/DuCrj<br>NIT : g<br>EPORT TYPE : A1 104<br>EX : FEMALE |             |          |              |      | BODY WEIGHT<br>ALL ANIMALS | CHANGES | (SUMMARY)  |       |      |      |          |      |          | PAGE : |
|--------------------------------------------------------------------------------------------|-------------|----------|--------------|------|----------------------------|---------|------------|-------|------|------|----------|------|----------|--------|
| roup Name                                                                                  | Admin<br>14 | istratio | n week<br>18 |      | 22                         |         | 26         |       | 30   |      | 34       |      | 38       |        |
| Control                                                                                    | 181±        | 11       | 190±         | 11   | 200±                       | 12      | 206±       | 12    | 213± | 13   | $221\pm$ | 14   | 228±     | 13     |
| 750 ppm                                                                                    | 178±        | 10       | 186±         | 10   | 198±                       | 11      | 204±       | 11    | 212± | 12   | 219±     | 12   | $226\pm$ | 13     |
| 1500 ppm                                                                                   | 173±        | 11**     | 180±         | 10** | 189±                       | 11**    | 193±       | 12**  | 199± | 13** | 206±     | 14** | 212±     | 14**   |
| 3000 ppm                                                                                   | 164±        | 10**     | 170±         | 9**  | 177±                       | 10**    | 179±       | 10**  | 184± | 11** | $189\pm$ | 12** | 193±     | 13**   |
|                                                                                            | . <u>p </u> |          |              |      |                            |         |            |       |      |      |          |      |          |        |
| Significant difference ;                                                                   | *:₽≦        | 0.05     | ** : P ≦ 0.0 | 01   |                            |         | Test of Du | nnett |      |      |          |      |          |        |
| AN260)                                                                                     |             |          |              |      |                            |         |            |       |      |      |          |      |          | BAIS   |

| STUDY NO. : 0267<br>ANIMAL : RAT F344/DuCrj<br>UNIT : g<br>REPORT TYPE : A1 104<br>SEX : FEMALE |      |           |             |      | BODY WEIGHT<br>ALL ANIMALS | CHANGES | (SUMMARY) |        |      |      |      |      |          | E    | PAGE : 10 |
|-------------------------------------------------------------------------------------------------|------|-----------|-------------|------|----------------------------|---------|-----------|--------|------|------|------|------|----------|------|-----------|
| Group Name                                                                                      |      | istration | woold       |      |                            |         |           |        |      |      |      |      |          | r    | AGE • 10  |
|                                                                                                 | 42   | ISUTALIUN | шеек<br>46  |      | 50                         |         | 54        |        | 58   |      | 62   |      | 66       |      |           |
| Control                                                                                         | 235± | 14        | 243±        | 16   | 249±                       | 16      | 258±      | 18     | 263± | 19   | 273± | 21   | 282±     | 22   |           |
| 750 ppm                                                                                         | 233± | 14        | 240±        | 15   | 245±                       | 14      | $253\pm$  | 15     | 258± | 15   | 268± | 18   | $274\pm$ | 18   |           |
| 1500 ppm                                                                                        | 217± | 16**      | 223±        | 16** | $225\pm$                   | 17**    | 233±      | 19**   | 236± | 19** | 242± | 22** | $248\pm$ | 23** |           |
| 3000 maga                                                                                       | 196± | 14**      | 200±        | 15** | 203±                       | 15**    | $205\pm$  | 16**   | 207± | 17** | 207± | 18** | $211\pm$ | 20** |           |
|                                                                                                 |      |           |             |      |                            |         |           |        |      |      |      |      |          |      |           |
| Significant difference ;                                                                        | *:Р≦ | 0.05      | ** : P ≦ 0. | 01   |                            |         | Test of D | unnett |      |      |      |      |          |      |           |
| (HAN260)                                                                                        |      |           |             |      |                            |         |           | ·····  |      |      |      |      | <u></u>  |      | BAIS 3    |

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| TUDY NO. : 0267<br>NIMAL : RAT F344/DuCrj<br>NIT : g<br>EPORT TYPE : A1 104<br>EX : FEMALE |          |           |         |      | BODY WEIGHT<br>ALL ANIMALS | CHANGES | (SUMMARY) |        |      |      |      |      |          | PAGE : 1 |
|--------------------------------------------------------------------------------------------|----------|-----------|---------|------|----------------------------|---------|-----------|--------|------|------|------|------|----------|----------|
| roup Name                                                                                  |          | istration |         |      |                            |         | ····      |        |      |      |      |      |          |          |
| ·                                                                                          | 70       |           | 74      |      | 78                         |         | 82        |        | 86   |      | 90   |      | 94       |          |
| Control                                                                                    | 292±     | 24        | 297±    | 24   | 305±                       | 24      | 311±      | 25     | 315± | 26   | 317± | 32   | $321\pm$ | 28       |
| 750 ppm                                                                                    | 283±     | 20        | 284±    | 21*  | 288±                       | 27**    | 297±      | 23*    | 300± | 22*  | 302± | 24*  | 300±     | 28**     |
| 1500 ppm                                                                                   | $251\pm$ | 25**      | 252±    | 27** | 254±                       | 29**    | 259±      | 30**   | 263± | 31** | 263± | 33** | 264±     | 32**     |
| 3000 ppm                                                                                   | 214±     | 20**      | 214±    | 22** | 217±                       | 21**    | 220±      | 23**   | 219± | 27** | 219± | 28** | 219±     | 30**     |
| Significant difference ;                                                                   | *:P≦     | 0.05      | **:P≦0. | 01   |                            |         | Test of D | unnett |      |      |      |      |          |          |

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| TUDY NO.: 0267<br>NIMAL : RAT F344/DLC-j<br>NIT : g<br>EPORT TYPE : A1 104 |         |          |             |      | BODY WEIGHT<br>ALL ANIMALS | CHANGES | (SUMMARY)       |      |          |
|----------------------------------------------------------------------------|---------|----------|-------------|------|----------------------------|---------|-----------------|------|----------|
| EX : FEMALE                                                                |         |          |             |      |                            |         |                 |      | PAGE : 1 |
| roup Name                                                                  |         | istratio |             |      |                            |         |                 | <br> | <br>     |
|                                                                            | 98      |          | 102         |      | 104                        |         |                 |      |          |
| Control                                                                    | 322±    | 30       | $321\pm$    | 43   | 322±                       | 36      |                 |      |          |
| 750 ppm                                                                    | 300±    | 35**     | 299±        | 36*  | 295±                       | 38**    |                 |      |          |
| 1500 ppm                                                                   | 265±    | 35**     | 269±        | 38** | 266±                       | 42**    |                 |      |          |
| 3000 ppm                                                                   | 217±    | 33**     | 219±        | 31** | 219±                       | 30**    |                 |      |          |
| Significant difference .                                                   | - · P - | 0.05     |             |      |                            |         |                 | <br> | <br>     |
| Significant difference ;<br>MAN260)                                        | *:15    | 0.05     | ** : P ≦ 0. | 01   |                            |         | Test of Dunnett | <br> | <br>     |
| ANLOV /                                                                    |         |          |             |      |                            |         |                 |      | BAIS     |

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APPENDIX C 1

WATER CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(2-YEAR STUDY)

STUDY NO. : 0267 ANIMAL : RAT F344/DuC-j UNIT : g REPORT TYPE : A1 104 SEX : MALE

### WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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| o Name                 | Administration     | week          |             |                 |             |             |             |
|------------------------|--------------------|---------------|-------------|-----------------|-------------|-------------|-------------|
|                        | 1                  | 2             | 3           | 4               | 5           | 6           | 7           |
| Control                | 17.1± 1.1          | 18.8± 3.4     | 18.8± 2.2   | 19.2± 2.2       | 18.2± 1.9   | 19.4± 2.9   | 19.9± 4.1   |
| 750 ppm                | 15.6± 2.8**        | 16.4± 4.2**   | 15.7± 1.7** | 15.7± 1.7**     | 14.7± 2.0** | 15.4± 1.8** | 15.6± 1.5** |
| 1500 ppm               | 13.5± 3.0**        | 13.2± 1.2**   | 13.7± 1.1** | 13.5± 1.3**     | 13.2± 1.5** | 13.6± 1.7** | 13.8± 1.7** |
| 3000 ppm               | 11.9± 0.8**        | 11.7± 0.8**   | 11.4± 0.9** | 11.7± 1.9**     | 10.9± 1.3** | 11.9± 1.9** | 11.5± 1.2** |
| Significant difference | : <b>*</b> :P≤0.05 | ** : P ≤ 0.01 |             | Test of Dunnett |             |             |             |

STUDY NO. : 0267 ANIMAL : RAT F344/Ducri UNIT : g REPORT TYPE : A1 104 SEX : MALE

Group Name

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

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| up Name  | Administration | week        |             |             |             |             | ****        |
|----------|----------------|-------------|-------------|-------------|-------------|-------------|-------------|
|          | 8              | 9           | 10          | 11          | 12          | 13          | 14          |
| Control  | 19.2± 2.4      | 18.5± 2.4   | 18.3± 3.2   | 18.1± 2.2   | 16.4± 1.8   | 18.7± 2.0   | 18.4± 1.9   |
| 750 ppm  | 15.5± 1.7**    | 15.7± 1.8** | 15.3± 2.1** | 15.7± 1.9** | 14.3± 1.6** | 16.1± 1.7** | 15.7± 1.8** |
| 1500 ppm | 13.5± 1.4**    | 13.6± 1.4** | 13.6± 1.5** | 13.9± 1.4** | 12.8± 1.3** | 14.4± 1.3** | 14.0± 1.3** |
| 3000 ppm | 11.4± 1.3**    | 11.7± 1.3** | 11.4± 1.2** | 11.6± 1.1** | 10.4± 0.9** | 12.1± 1.1** | 11.8± 1.1** |

Test of Dunnett

(HAN260)

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

WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS -

STUDY NO. : 0267 ANIMAL : RAT F344/DuC-j UNIT : g REPORT TYPE : A1 104 SEX : MALE

PAGE: 3

| p Name                 | Administration | week          |             |                 |             |             |             |
|------------------------|----------------|---------------|-------------|-----------------|-------------|-------------|-------------|
|                        | 18             | 22            | 26          | 30              | 34          | 38          | 42          |
| Contral                | 17.9± 1.6      | 18.0± 1.4     | 18.4± 1.5   | 18.5± 1.2       | 17.8± 1.3   | 18.3± 1.2   | 18.2± 1.8   |
| 750 ppm                | 15.9± 1.3**    | 16.2± 1.5**   | 16.1± 1.1** | 16.2± 1.5**     | 16.0± 1.0** | 16.5± 1.0** | 16.2± 1.1** |
| 1500 ppm               | 13.9± 1.1**    | 13.8± 1.2**   | 14.4± 0.9** | 14.5± 1.0**     | 14.3± 1.5** | 14.3± 1.0** | 14.2± 1.1** |
| 3000 ppm               | 11.8± 0.9**    | 11.7± 1.0**   | 11.8± 1.0** | 12.0± 0.8**     | 11.8± 0.8** | 12.1± 0.9** | 11.7± 0.9** |
| Significant difference | ; *:P≤0.05     | ** : P ≤ 0.01 |             | Test of Dunnett |             |             | ······      |
| izeo)                  | , + · r ≧ 0.05 | ** · r ⊇ v.vi |             |                 |             |             |             |

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WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj UNIT : g REPORT TYPE : A1 104 SEX : MALE

PAGE: 4

| oup Name                 | Administration | week          |             |                 |             | ·····       | ······································ |
|--------------------------|----------------|---------------|-------------|-----------------|-------------|-------------|----------------------------------------|
| - wat                    | 46             | 50            | 54          | 58              | 62          | 66          | 70                                     |
| Control                  | 18.1± 1.2      | 18.4± 1.4     | 17.6± 1.7   | 18.0± 1.5       | 18.6± 1.6   | 19.6± 1.7   | 19.7± 1.9                              |
| 750 ppm                  | 16.3± 1.1**    | 16.5± 1.0**   | 16.2± 1.2*  | 16.7± 1.1*      | 17.4± 1.2*  | 17.8± 1.3** | 18.2± 1.5*                             |
| 1500 ppm                 | 14.4± 1.1**    | 14.7± 1.1**   | 14.4± 1.1** | 14.5± 1.6**     | 15.3± 1.3** | 15.5± 1.2** | 16.2± 1.2**                            |
| 3000 ppm                 | 11.9± 0.9**    | 12.2± 1.3**   | 12.1± 0.9** | 12.1± 0.8**     | 12.6± 0.8** | 12.8± 1.1** | 13.4± 1.3**                            |
|                          |                |               |             |                 |             |             | ·                                      |
| Significant difference ; | *:P≦ 0.05      | ** : P ≦ 0.01 |             | Test of Dunnett |             |             |                                        |

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(HAN260)

STUDY NO.: 0267 ANIMAL: RAT F344/DuCrj UNIT: g REPORT TYPE: A1 104 SEX: MALE

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

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PAGE: 5

| up Name                | Administration   | week_         |             |                 |             |             |             |
|------------------------|------------------|---------------|-------------|-----------------|-------------|-------------|-------------|
|                        | 74               | 78            | 82          | 86              | 90          | 94          | 98          |
| Control                | 20.9± 3.5        | 21.0± 2.4     | 21.4± 2.8   | 20.7± 4.5       | 22.5± 3.2   | 23.5± 5.8   | 24.1± 7.3   |
| 750 ppm                | 18.7± 1.8*       | 19.1± 2.2     | 18.9± 2.4*  | 19.3± 2.9       | 19.5± 3.9*  | 20.6± 4.0   | 20.5± 4.1   |
| 1500 ppm               | 16.2± 1.4**      | 16.3± 1.5**   | 15.2± 2.9** | 15.6± 2.4**     | 16.1± 2.1** | 16.3± 2.2** | 16.0± 2.7** |
| 3000 ppm               | 13.4± 1.3**      | 13.1± 1.1**   | 12.6± 1.7** | 12.6± 2.2**     | 13.3± 1.5** | 13.3± 1.6** | 13.7± 1.6** |
|                        |                  |               |             |                 |             |             |             |
| Significant difference | $*: P \leq 0.05$ | ** : P ≦ 0.01 |             | Test of Dunnett |             |             |             |
| AN260)                 |                  |               |             |                 |             | <u></u>     |             |

STUDY NO. : 0267 WATER CONSUMPTION CHANGES (SUMMARY) ANIMAL : RAT F344/DuCrj ALL ANIMALS UNIT : g REPORT TYPE : A1 104 SEX : MALE PAGE: 6 Group Name Administration week\_ 102 104 Control  $25.2 \pm 7.4$  $23.5 \pm 7.0$ 750 ppm 20.8± 4.9  $21.3\pm$  6.0 1500 ppm 15.7± 2.1\*\* 16.5± 2.7\*\* 3000 ppm 13.3± 1.9\*\* 14.1± 2.2\*\* Significant difference ;  $*: P \leq 0.05$ \*\* : P ≦ 0.01 Test of Dunnett (HAN260) BAIS 3

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### APPENDIX C 2

## WATER CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(2-YEAR STUDY)

STUDY NO.: 0267 ANIMAL: RAT F344/DuCrj UNIT: g REPORT TYPE: A1 104 SEX: FEMALE

### WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE: 7

| oup Name               | Administration | week          | · · · · · · · · · · · · · · · · · · · |                 |             |             |             |
|------------------------|----------------|---------------|---------------------------------------|-----------------|-------------|-------------|-------------|
|                        | 1              | 2             | 3                                     | 4               | 5           | 6           | 7           |
| Control                | 14.5± 1.0      | 17.8± 3.5     | 17.1± 4.3                             | 18.1± 4.3       | 19.0± 8.5   | 19.9± 8.0   | 19.4± 6.9   |
| 750 ppm                | 13.1± 2.2**    | 13.4± 2.1**   | 12.9± 2.1**                           | 12.7± 1.8**     | 12.7± 2.4** | 12.5± 2.3** | 12.2± 1.6** |
| 1500 ppm               | 10.7± 0.9**    | 10.7± 1.1**   | 10.5± 1.4**                           | 10.3± 1.2**     | 10.2± 1.1** | 9.9± 1.3**  | 10.3± 1.8** |
| 3000 ppm               | 9.8± 2.5**     | 9.8± 1.7**    | 8.9± 0.8**                            | 9.1± 1.1**      | 9.0± 1.1**  | 8.9± 1.3**  | 9.3± 2.4**  |
| Significant difference | ; *:P≦0.05     | ** : P ≤ 0.01 |                                       | Test of Dunnett |             |             |             |

WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS ,

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STUDY NO. : 0267 ANIMAL : RAT F344/DuC-j UNIT : g REPORT TYPE : A1 104 SEX : FEMALE

PAGE: 8

| oup Name                 | Administration week |               |             |                 |             |             |             |  |
|--------------------------|---------------------|---------------|-------------|-----------------|-------------|-------------|-------------|--|
|                          | 8                   | 9             | 10          | 11              | 12          | 13          | 14          |  |
| Control                  | 15.9± 3.7           | 15.3± 3.7     | 19.0± 9.3   | 17.8± 5.5       | 18.7± 8.9   | 19.8± 8.3   | 20.3± 8.3   |  |
| 750 ppm                  | 11.5± 1.8**         | 11.9± 3.0**   | 12.8± 5.0** | 12.8± 3.0**     | 12.4± 3.3** | 14.4± 6.4** | 14.0± 5.0** |  |
| 1500 ppm                 | 9.4± 1.6**          | 9.3± 1.3**    | 10.0± 1.6** | 9.9± 1.2**      | 9.5± 1.2**  | 10.4± 3.1** | 10.5± 4.4** |  |
| 3000 ppm                 | 8.4± 2.2**          | • 7.7± 0.9**  | 8.6± 0.9**  | 8.6± 1.0**      | 8.1± 1.0**  | 8.6± 1.0**  | 8.6± 1.2**  |  |
| Significant difference : | ; *:P≦0.05          | ** : P ≤ 0.01 |             | Test of Dunnett |             | <i></i>     |             |  |

WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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STUDY NO. : 0267 ANIMAL : RAT F344/DuC-j UNIT : g REPORT TYPE : A1 104 SEX : FEMALE

PAGE: 9

| o Name                | Administration                        | week          |             |                 |             |             |             |
|-----------------------|---------------------------------------|---------------|-------------|-----------------|-------------|-------------|-------------|
|                       | 18                                    | 22            | 26          | 30              | 34          | 38          | 42          |
| Control               | 16.7± 4.0                             | 21.1± 8.1     | 21.1± 8.5   | 20.2± 8.4       | 19.6± 8.1   | 19.1± 6.4   | 17.1± 4.0   |
| 750 ppm               | 12.3± 2.5**                           | 15.1± 6.6**   | 15.8± 5.4** | 15.5± 5.4*      | 15.5± 6.5** | 16.0± 5.7*  | 14.4± 5.6** |
| 1500 ppm              | 9.7± 1.8**                            | 10.4± 1.2**   | 11.3± 1.6** | 10.9± 1.9**     | 11.4± 2.1** | 11.4± 2.7** | 10.6± 0.9** |
| 3000 ppm              | 8.1± 1.0**                            | 9.0± 1.5**    | 9.6± 1.4**  | 9.7± 2.2**      | 9.8± 1.5**  | 10.0± 2.1** | 9.8± 2.1**  |
| Ci                    |                                       |               |             |                 |             |             |             |
| Significant differenc | xe; *:P≦0.05 ::                       | ** : P ≦ 0.01 |             | Test of Dunnett |             |             |             |
|                       | · · · · · · · · · · · · · · · · · · · |               |             |                 |             |             | _           |

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj UNIT : g REPORT TYPE : A1 104 SE

### WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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| Group Name | Administration | week        |             |                     |             |             |             |  |
|------------|----------------|-------------|-------------|---------------------|-------------|-------------|-------------|--|
|            | 46             | 50          | 54          | 58                  | 62          | 66          | 70          |  |
| Control    | 17.5± 5.7      | 16.7± 3.4   | 17.0± 4.6   | 15.9± 3.3           | 17.2± 4.3   | 17.8± 5.0   | 17.9± 3.3   |  |
| 750 ppm    | 15.0± 6.7**    | 13.9± 2.5** | 15.4± 5.3*  | 13.9± 3.4**         | 15.0± 3.3** | 14.9± 4.3** | 14.5± 2.2** |  |
| 1500 ppm   | 10.9± 1.7**    | 10.7± 1.6** | 11.8± 3.0** | 11 <b>.7± 2.5**</b> | 12.6± 2.8** | 12.7± 3.1** | 13.7± 3.3** |  |
| 3000 ppm   | 10.2± 2.6**    | 10.7± 2.5** | 11.5± 3.7** | 11.3± 2.9**         | 12.5± 3.1** | 12.6± 3.0** | 13.4± 3.0** |  |

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| Significant difference ; | *:P ≦ 0.05 | ** : P ≦ 0.01 | Test of Durnett |  |
|--------------------------|------------|---------------|-----------------|--|
| (HAN260)                 |            |               |                 |  |

WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS -\_\_\_\_

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STUDY NO.: 0267 ANIMAL : RAT F344/DuCrj UNIT : g REPORT TYPE : A1 104 SEX : FEMALE

PAGE: 11

| up Name                | Administration | week          |             |                 |             |             |             |
|------------------------|----------------|---------------|-------------|-----------------|-------------|-------------|-------------|
|                        | 74             | 78            | 82          | 86              | 90          | 94          | 98          |
| Control                | 18.1± 3.8      | 19.2± 3.9     | 18.8± 4.6   | 18.5± 4.4       | 20.2± 5.1   | 20.4± 5.0   | 20.6± 4.6   |
| 750 ppm                | 14.9± 3.6**    | 14.9± 3.3**   | 14.8± 3.0** | 15.3± 3.3**     | 16.4± 3.1** | 15.5± 3.9** | 15.8± 3.3** |
| 1500 ppm               | 13.9± 4.0**    | 14.8± 3.7**   | 14.7± 4.0** | 15.8± 4.2**     | 16.6± 4.7** | 17.7± 4.9** | 17.5土 4.7** |
| 3000 ppm               | 13.4± 2.6**    | 13.8± 2.5**   | 14.3± 2.6** | 14.1± 2.9**     | 16.2± 5.1** | 16.0± 3.4** | 15.6± 3.7** |
|                        |                |               |             |                 |             |             |             |
| Significant difference | e; *:P≦0.05 >  | ** : P ≦ 0.01 |             | Test of Dunnett |             |             |             |
| N260)                  |                |               |             |                 |             |             |             |

| .Grj           |                                                                               |                                                                                                                                                                                                                                           | PAGE: 12                  |
|----------------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|
| Administration | week                                                                          |                                                                                                                                                                                                                                           |                           |
| 102            | 104                                                                           |                                                                                                                                                                                                                                           |                           |
| 20.5± 4.8      | 21.0± 4.0                                                                     |                                                                                                                                                                                                                                           |                           |
| 15.5土 4.0**    | 16.2± 4.8**                                                                   |                                                                                                                                                                                                                                           |                           |
| 18.1± 5.2      | 18.0± 5.9**                                                                   |                                                                                                                                                                                                                                           |                           |
| 15.4± 5.2**    | 15.7± 2.7**                                                                   |                                                                                                                                                                                                                                           |                           |
|                |                                                                               |                                                                                                                                                                                                                                           |                           |
| ence; *:P≧0.05 | *** : P ≥ 0.01                                                                | lest of Junnett                                                                                                                                                                                                                           | BAISS                     |
|                | Administration<br>102<br>20.5± 4.8<br>15.5± 4.0**<br>18.1± 5.2<br>15.4± 5.2** | Administration       week         102       104         20.5 $\pm$ 4.8       21.0 $\pm$ 4.0         15.5 $\pm$ 4.0**       16.2 $\pm$ 4.8**         18.1 $\pm$ 5.2       18.0 $\pm$ 5.9**         15.4 $\pm$ 5.2**       15.7 $\pm$ 2.7** | Administration       week |

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### APPENDIX D 1

### FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(2-YEAR STUDY)

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj UNIT : g REPORT TYPE : A1 104 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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PAGE: 1

| roup Name | Administration<br>1-7(7) | week-day(effective)<br>2-7(7) | 3-7(7)      | 4-7(7)      | 5-7(7)         | 6-7(7)      | 7-7(7)      |
|-----------|--------------------------|-------------------------------|-------------|-------------|----------------|-------------|-------------|
|           |                          |                               | - • • • •   |             |                |             |             |
| Control   | 13.2± 0.8                | 14.4± 1.0                     | 14.8± 1.1   | 15.3± 1.3   | $15.0 \pm 1.5$ | 15.0± 1.6   | 15.2± 1.7   |
| 750 ppm   | 12.9± 0.9                | 14.4± 1.1                     | 14.5± 1.0   | 14.9± 1.5   | 14.1± 1.4**    | 14.2± 1.6*  | 14.4± 1.4*  |
| 1500 pom  | 12.2± 0.6**              | 13.7± 0.9**                   | 14.2± 1.0** | 14.1± 1.3** | 14.1± 1.4**    | 14.2± 1.8*  | 14.5± 1.6   |
| 3000 ppm  | 10.5± 0.7**              | 13.1± 0.8**                   | 13.2± 0.9** | 13.0± 1.1** | 12.9± 1.3**    | 13.2± 1.4** | 13.2± 1.5** |

(HAN260)

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj UNIT : g REPORT TYPE : A1 104 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)     | 14-7(7)                               |
| Control  | 14.9± 1.7      | 14.7± 1.7           | 14.7± 1.7   | 15.0± 1.7       | 14.3± 1.6   | 15.3± 1.7   | 14.5± 1.6                             |
| 750 mag  | 14.1± 1.5*     | 14.3± 1.3           | 14.1± 1.3   | $14.5 \pm 1.5$  | 13.8± 1.2   | 14.8± 1.2   | 14.1± 1.2                             |
| 1500 mag | 14.3± 1.5      | 14.4± 1.4           | 14.2± 1.4   | 14.6± 1.3       | 14.0± 1.2   | 14.9± 1.3   | 14.3± 1.3                             |
| 3000 ppm | 12.9± 1.4**    | 13.3± 1.3**         | 12.8± 1.1** | 13.2± 1.1**     | 12.7± 1.0** | 13.6± 1.1** | 13.1± 1.1**                           |
|          |                |                     |             |                 |             |             |                                       |
|          | nce; *:P≦0.05  | ** : P ≦ 0.01       |             | Test of Dunnett |             |             |                                       |
| 260)     |                |                     |             |                 |             |             | BAIS3                                 |

| ANIMAL : RAT F344/DuCrj |
|-------------------------|
| UNIT : g                |
| REPORT TYPE : A1 104    |
| SEX : MALE              |

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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PAGE: 3

| roup Name                | Administration<br>18-7(7) | week-day(effective)<br>22-7(7) | 26-7(7)     | 30-7(7)                                | 34-7(7)     | 38-7(7)     | 42-7(7)     |
|--------------------------|---------------------------|--------------------------------|-------------|----------------------------------------|-------------|-------------|-------------|
| Control                  | 14.9± 1.2                 | 15.1± 1.2                      | 15.6± 1.1   | 15.6± 1.0                              | 15.7± 1.0   | 15.7± 1.0   | 15.9± 1.2   |
| 750 ppm                  | 14.5± 1.0                 | 15.0± 0.9                      | 15.3± 1.0   | 15.4± 1.0                              | 15.4± 0.9   | 15.7± 0.9   | 15.8± 0.9   |
| 1500 ppm                 | 14.5± 1.1                 | 14.8± 1.2                      | 15.2± 1.0   | 15.3± 0.9                              | 14.9± 0.8** | 15.2± 1.0*  | 15.4± 1.1   |
| 3000 ppm                 | 13.4± 1.1**               | 13.5± 1.1**                    | 13.6± 1.0** | 13.9± 1.0**                            | 13.6± 0.9** | 14.0± 1.0** | 14.0± 1.1** |
| Significant difference ; | *:P ≤ 0.05                | ** : P ≤ 0.01                  |             | Test of Dunnett                        |             |             |             |
| N260)                    |                           | - <u> </u>                     |             | ······································ |             |             |             |

| Dup Name | Administration | week-day(effective) |             |             |             |             |             |
|----------|----------------|---------------------|-------------|-------------|-------------|-------------|-------------|
|          | 46-7(7)        | 50-7(7)             | 54-7(7)     | 58-7(7)     | 62-7(7)     | 66-7(7)     | 70-7(7)     |
| Control  | 16.2± 1.0      | 15.9± 1.1           | 15.8± 1.0   | 15.8± 0.9   | 16.6± 1.1   | 17.0± 1.2   | 17.1± 1.4   |
| 750 ppm  | 16.0± 0.9      | 15.7± 0.8           | 16.0± 0.8   | 15.8± 0.9   | 16.7± 1.0   | 16.8± 0.9   | 16.8± 1.0   |
| 1500 ppm | 15.5± 0.9**    | 15.2± 0.9*          | 15.7± 0.8   | 15.5± 1.0   | 16.3± 0.9   | 16.4± 1.0   | 16.4± 1.0** |
| 3000 ppm | 14.3± 1.0**    | 13.9± 1.0**         | 14.7± 1.0** | 14.3± 0.8** | 14.7± 1.0** | 14.9± 1.2** | 15.0± 0.9** |

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| STUDY NO.: 0267<br>ANIMAL : RAT F344/DuGrj<br>UNIT : g<br>REPORT TYPE : A1 104 |                           |                                |             |                 |             |             |             |  |
|--------------------------------------------------------------------------------|---------------------------|--------------------------------|-------------|-----------------|-------------|-------------|-------------|--|
| SEX : MALE                                                                     |                           |                                |             |                 |             |             | PAGE :      |  |
| Group Name                                                                     | Administration<br>74-7(7) | week-day(effective)<br>78-7(7) | 82-7(7)     | 86-7(7)         | 90-7(7)     | 94-7(7)     | 98-7(7)     |  |
| Control                                                                        | 16.5± 1.6                 | 16.9± 1.4                      | 16.6± 1.3   | $15.7\pm$ 2.8   | 16.4± 1.4   | 16.1± 1.6   | 15.8± 2.6   |  |
| 750 ppm                                                                        | 16.7± 1.2                 | 16.8± 1.1                      | 16.5± 1.1   | 16.5± 1.1       | 15.9± 1.5   | 16.5± 1.2   | 16.2± 1.5   |  |
| 1500 ppm                                                                       | 16.3± 1.3                 | 16.2± 1.3*                     | 15.1± 6.7   | 15.8± 1.1       | 15.5± 1.4** | 15.9± 1.1   | 15.5± 1.9   |  |
| 3000 ppm                                                                       | 14.5± 1.2**               | 14.3± 1.3**                    | 13.6± 2.6** | 14.0± 1.3**     | 14.1± 1.1** | 14.1± 1.2** | 13.7± 1.3** |  |
| Significant difference ;                                                       | *:P ≤ 0.05                | ** : P ≦ 0.01                  |             | Test of Dunnett |             |             |             |  |
| (HAN260)                                                                       |                           |                                |             |                 |             |             | BAISS       |  |

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| Significant difference ;                                                                      | *:P≦ 0.05                  | ** : P ≦ 0.01                    | Test of Durnett                                   |         |
|-----------------------------------------------------------------------------------------------|----------------------------|----------------------------------|---------------------------------------------------|---------|
| 3000 ppm                                                                                      | 13.9± 1.3**                | 13.7± 1.4**                      |                                                   |         |
| 1500 ppm                                                                                      | 15.5± 1.3                  | 15.2± 1.8                        |                                                   |         |
| 750 ppm                                                                                       | 16.1± 1.5                  | 15.8± 1.8                        |                                                   |         |
| Control                                                                                       | 15.3± 2.5                  | 15.7± 2.0                        |                                                   |         |
| Group Name                                                                                    | Administration<br>102-7(7) | week-day(effective)_<br>104-7(7) |                                                   |         |
| STUDY NO. : 0267<br>ANIMAL : RAT F344/DuCrj<br>UNIT : g<br>REPORT TYPE : A1 104<br>SEX : MALE |                            |                                  | FOOD CONSUMPTION CHANGES (SUMMARY)<br>ALL ANIMALS | PAGE: 6 |

### APPENDIX D 2

# FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(2-YEAR STUDY)

| STUDY NO. : 0267        |
|-------------------------|
| ANIMAL : RAT F344/DuCrj |
| UNIT : g                |
| REPORT TYPE : A1 104    |
| SEX : FEMALE            |
|                         |

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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PAGE: 7

| oup Name               | Administration<br>1-7(7) | week-day(effective)<br>2-7(7) | 3-7(7)      | 4-7(7)          | 5-7(7)     | 6-7(7)     | 7-7(7)     |
|------------------------|--------------------------|-------------------------------|-------------|-----------------|------------|------------|------------|
| Control                | 10.5± 0.5                | 10.9± 0.6                     | 10.9± 0.7   | 10.6± 0.7       | 10.5± 0.8  | 10.0± 0.9  | 10.0± 0.8  |
| 750 mag                | 10.3± 0.7                | 10.6± 0.9                     | 10.5± 0.9   | 10.2± 0.9       | 10.1± 1.1* | 9.5± 1.1*  | 9.6± 1.0   |
| 1500 ppm               | 9.6± 0.5**               | 10.2± 0.8**                   | 10.2± 0.8** | 9.9± 0.8**      | 9.6± 1.0** | 9.3± 1.1** | 9.4± 1.0** |
| 3000 maa               | 8.3± 0.6**               | 9.8± 0.7**                    | 9.6± 0.7**  | 9.3± 1.0**      | 9.3± 0.8** | 8.8± 0.9** | 9.1± 0.9** |
| Significant difference | ; *:P≦0.05 ;             | ** : P ≦ 0.01                 |             | Test of Dunnett |            |            |            |
| AN260)                 | ····                     |                               |             |                 |            |            |            |

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj UNIT : g REPORT TYPE : A1 104 SEX : FEMALE FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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PAGE: 8

| up Name  | Administration<br>8-7(7) | week-day(effective)<br>9-7(7) | 10-7(7)    | 11-7(7)    | 12-7(7)    | 13-7(7)    | 14-7(7)    |
|----------|--------------------------|-------------------------------|------------|------------|------------|------------|------------|
| Control  | 9.7± 0.8                 | 9.8± 0.8                      | 9.6± 0.9   | 9.6± 1.1   | 9.5± 1.0   | 9.7± 0.9   | 9.6± 1.0   |
| 750 ppm  | 9.4± 1.0                 | 9.4± 0.9                      | 9.3± 1.0   | 9.4± 0.9   | 9.2± 1.0   | 9.3± 0.8   | 9.2± 0.8   |
| 1500 ppm | 9.0± 1.1**               | 9.1± 1.0**                    | 8.9± 1.0** | 9.0± 1.0** | 8.6± 0.9** | 9.2± 0.9** | 9.0± 0.9** |
| 3000 ppm | 8.7± 0.9**               | 8.5± 0.9**                    | 8.5± 0.8** | 8.6± 0.9** | 6.9± 0.8** | 8.6± 0.8** | 8.5± 0.8** |

(HAN260)

| up Name                                | Administration week-day(effective) |               |            |                 |             |             |             |  |
|----------------------------------------|------------------------------------|---------------|------------|-----------------|-------------|-------------|-------------|--|
| ······································ | 18-7(7)                            | 22-7(7)       | 26-7(7)    | 30-7(7)         | 34-7(7)     | 38-7(7)     | 42-7(7)     |  |
| Contral                                | 9.8± 0.8                           | 10.3± 0.8     | 10.5± 0.8  | 10.8± 0.8       | 11.0± 0.9   | 11.2± 0.7   | 11.2± 0.9   |  |
| 750 ppm                                | 9.5± 0.7                           | 10.1± 0.8     | 10.4± 0.7  | 10.8± 0.7       | 10.8± 0.7   | 11.2± 0.8   | 11.1± 0.8   |  |
| 1500 ppm                               | 9.1± 0.7**                         | 9.6± 0.8**    | 9.8± 0.9** | 10.0± 0.9**     | 10.2± 0.8** | 10.4± 0.8** | 10.2± 0.9** |  |
| 3000 maa                               | 8.6± 0.7**                         | 8.9± 0.7**    | 9.1± 0.7** | 9.4± 0.7**      | 9.4± 0.8**  | 9.5± 0.9**  | 9.5± 0.8**  |  |
| Significant difference ;               | *:P ≤ 0.05                         | ** : P ≤ 0.01 |            | Test of Dunnett |             |             |             |  |

FOOD CONSUMPTION CHANGES (SUMMARY)

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ALL ANIMALS

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj UNIT : g REPORT TYPE : A1 104

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| p Name   | Adminis<br>46-7(7 | tration<br>) | week-day(effective)<br>50-7(7) | 54-7(7)     | 58-7(7)     | 62-7(7)     | 66-7(7)     | 70–7 (7)    |
|----------|-------------------|--------------|--------------------------------|-------------|-------------|-------------|-------------|-------------|
| Contral  | 11.5± 1           | .0           | 11.3± 0.8                      | 11.7± 0.8   | 11.2± 0.9   | 12.0± 1.1   | 12.5± 1.0   | 12.7± 1.0   |
| 750 pom  | 11.2± 0           | .8           | 11.4± 0.8                      | 11.6± 0.8   | 11.0± 0.7   | 12.0± 0.9   | 12.4± 0.8   | 12.4± 0.9   |
| 1500 ppm | 10.6± 0           | .8**         | 10.4± 0.9**                    | 11.0± 0.9** | 10.6± 0.8** | 11.2± 1.0** | 11.7± 1.0** | 11.7± 1.2** |
| 3000 ppm | 9.7± 0            | .8**         | 9.6± 0.8**                     | 9.9± 0.9**  | 9.8± 1.0**  | 10.0± 1.3** | 10.7± 1.2** | 10.6± 1.5** |

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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STUDY NO. : 0267

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| STUDY NO. : 0267       |    |
|------------------------|----|
| ANIMAL : RAT F344/DuCr | -j |
| UNIT : g               |    |
| REPORT TYPE : A1 104   |    |
| SEX : FEMALE           |    |
|                        |    |

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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PAGE : 11

| Control 12.  |          |             |                |                |             |             |                |
|--------------|----------|-------------|----------------|----------------|-------------|-------------|----------------|
|              | 6± 1.0   | 12.6± 1.0   | $12.4 \pm 1.4$ | $12.7 \pm 1.3$ | 12.6± 1.8   | 12.9± 2.1   | $12.6 \pm 1.9$ |
| 750 ppm 12.  | 3± 1.1   | 12.3± 1.2   | 12.4± 1.2      | 12.7± 1.5      | 12.3± 2.6   | 13.2± 2.5   | 12.9± 1.9      |
| 1500 ppm 11. | 9± 1.2*  | 11.9± 1.2*  | 11.9± 1.3      | 12.3± 1.7      | 12.0± 1.8*  | 12.5± 1.6   | 12.5± 1.9      |
| 3000 ppm 10. | 6± 1.6** | 10.6± 1.2** | 10.8± 1.2**    | 10.5± 1.4**    | 10.8± 1.3** | 11.1± 1.5** | 10.8± 1.8**    |

(HAN260)

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| STUDY NO.: 0267<br>ANIMAL : RAT F344/DuGrj<br>UNIT : g<br>REPORT TYPE : A1 104 |  |                                 | FOOD CONSUMPTION CHANGES (SUMMARY)<br>ALL ANIMALS |           |
|--|--|---------------------------------|---|-----------|
| SEX : FEMALE   |  |                                 |   | PAGE : 12 |
| Group Name   | Administration<br>102-7(7)             | week-day(effective)<br>104-7(7) | )   |           |
| Control  | 12.5± 2.8                              | 12.4± 2.0                       |   |           |
| 750 ppm  | 12.9± 2.6                              | 12.0± 2.7                       |   |           |
| 1500 ppm   | 12.7± 1.7                              | 12.1± 1.9                       |   |           |
| 3000 ppm   | 10.7± 1.4**                            | 10.3± 1.8**                     |   |           |
|  |  |                                 |   |           |
| Significant difference ;   | *:P≦ 0.05                              | ** : P ≦ 0.01                   | Test of Dunnett                                   |           |
| (HAN260)   | ······································ |                                 |   | BAIS 3    |

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APPENDIX E 1

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : MALE

STUDY NO.: 0267 ANIMAL: RAT F344/DuCrj UNIT: g/kg/day REPORT TYPE: A1 104 SEX: MALE

CHEMICAL INTAKE CHANGES (SUMMARY)

ALL ANIMALS

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PAGE: 1

1

| -oup Name | Administration (weeks) |              |              |              |              |              |              |  |
|-----------|------------------------|--------------|--------------|--------------|--------------|--------------|--------------|--|
|           | 1                      | 2            | 3            | 4            | 5            | 6            | 7            |  |
| Control   | 0.000± 0.000           | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 |  |
| 750 ppm   | 0.078± 0.014           | 0.070± 0.018 | 0.060± 0.006 | 0.056± 0.004 | 0.049± 0.005 | 0.048± 0.003 | 0.046± 0.003 |  |
| 1500 ppm  | 0.139± 0.030           | 0.117± 0.008 | 0.108± 0.006 | 0.098± 0.005 | 0.089± 0.006 | 0.086± 0.006 | 0.083± 0.006 |  |
| 3000 ppm  | 0.263± 0.016           | 0.222± 0.011 | 0.195± 0.010 | 0.185± 0.026 | 0.160± 0.013 | 0.165± 0.021 | 0.153± 0.009 |  |

(HAN300)

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|                |   |   | (SUMMARY)  |  |   | PAGE : 2   |  |
|----------------|---|---|--|--|---|--|--|
| Administration | (weeks)   | 10  |  | 10   | 10  |  |  |
|                | 3   | 10  | 11   | 12   |   | 14   |  |
| 0.000± 0.000   | 0.000± 0.000                                      | 0.000± 0.000  | 0.000± 0.000   | 0.000± 0.000   | 0.000± 0.000  | 0.000± 0.000   |  |
| 0.044± 0.003   | 0.043± 0.003                                      | 0.041± 0.004  | 0.041± 0.004   | 0.036± 0.004   | 0.040± 0.003  | 0.038± 0.004   |  |
| 0.079± 0.005   | 0.076± 0.004                                      | 0.073± 0.004  | 0.073± 0.004   | 0.065± 0.005   | 0.072± 0.005  | 0.069± 0.004   |  |
| 0.146± 0.010   | 0.143± 0.010                                      | 0.135± 0.010  | 0.134± 0.008   | 0.119± 0.008   | 0.134± 0.008  | 0.128± 0.008   |  |
|                | 8<br>0.000± 0.000<br>0.044± 0.003<br>0.079± 0.005 | Administration (weeks)<br>8 9 0.000± 0.000 0.000± 0.000 0.044± 0.003 0.043± 0.003 0.079± 0.005 0.076± 0.004 | ALL ANIMALS<br>Administration (weeks)<br>8 $9$ 10<br>0.000 $\pm$ 0.000 $0.000 \pm$ 0.000 $0.000 \pm$ 0.000<br>0.004 $\pm$ 0.003 $0.043 \pm$ 0.003 $0.041 \pm$ 0.004<br>0.079 $\pm$ 0.005 $0.076 \pm$ 0.004 $0.073 \pm$ 0.004 | ALL ANIMALS         Administration (weeks)         8       9       10       11 $0.000 \pm 0.000$ $0.000 \pm 0.000$ $0.000 \pm 0.000$ $0.000 \pm 0.000$ $0.004 \pm 0.003$ $0.043 \pm 0.003$ $0.041 \pm 0.004$ $0.041 \pm 0.004$ $0.079 \pm 0.005$ $0.076 \pm 0.004$ $0.073 \pm 0.004$ $0.073 \pm 0.004$ | ALL ANIMALS         Administration       (weeks)         8       9       10       11       12 $0.000 \pm 0.000$ $0.004 \pm 0.003$ $0.043 \pm 0.003$ $0.041 \pm 0.004$ $0.041 \pm 0.004$ $0.036 \pm 0.004$ $0.079 \pm 0.005$ $0.076 \pm 0.004$ $0.073 \pm 0.004$ $0.073 \pm 0.004$ $0.065 \pm 0.005$ | ALL ANIMALS         Administration (weeks)         8       9       10       11       12       13         0.000 $\pm$ 0.000       0.000 $\pm$ 0.000 |  |

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(HAN300)

| STUDY NO.: 20267<br>ANIMAL : RAT F344/DuCrj<br>UNIT : g/kg/day<br>REPORT TYPE : A1 104<br>SEX : MALE |                      |               | CHEMICAL INTAKE CHANGES<br>ALL ANIMALS | (SUMMARY)    |              |              | PAGE :       | 3 |
|--|----------------------|---------------|--|--------------|--------------|--------------|--------------|---|
| Group Name   | Administration<br>18 | (weeks)<br>22 | 26                                     | 30           | 34           | 38           | 42           |   |
| Control  | 0.000± 0.000         | 0.000± 0.000  | 0.000± 0.000                           | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 |   |
| 750 ppm  | 0.036± 0.003         | 0.035± 0.003  | 0.033± 0.002                           | 0.032± 0.003 | 0.030± 0.002 | 0.030± 0.002 | 0.029± 0.001 |   |
| 1500 ppm   | 0.064± 0.003         | 0.060± 0.003  | 0.060± 0.003                           | 0.058± 0.003 | 0.056± 0.006 | 0.055± 0.003 | 0.053± 0.003 |   |
| 3000 ppm   | 0.121± 0.005         | 0.113± 0.006  | 0.110± 0.006                           | 0.108± 0.006 | 0.103± 0.005 | 0.103± 0.005 | 0.098± 0.006 |   |

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(HAN300)

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| STUDY NO.: 0267<br>ANIMAL : RAT F344/DuCrj<br>UNIT : g/kg/day<br>REPORT TYPE : A1 104<br>SEX : MALE |                |              | HEMICAL INTAKE CHANGES<br>LL ANIMALS | (SUMMARY)    |              |              | PAGE: 4      |
|---|----------------|--------------|--------------------------------------|--------------|--------------|--------------|--------------|
| Group Name  | Administration | (weeks)      |                                      |              |              | ····         |              |
|   | 46             | 50           | 54                                   | 58           | 62           | 66           | 70           |
| Control   | 0.000± 0.000   | 0.000± 0.000 | 0.000± 0.000                         | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 |
| 750 ppm   | 0.028± 0.002   | 0.028± 0.001 | 0.027± 0.002                         | 0.028± 0.002 | 0.028± 0.002 | 0.029± 0.002 | 0.029± 0.002 |
| 1500 ppm  | 0.052± 0.002   | 0.052± 0.003 | 0.051± 0.003                         | 0.050± 0.005 | 0.052± 0.003 | 0.052± 0.003 | 0.055± 0.004 |
| 3000 ppm  | 0.097± 0.006   | 0.099± 0.012 | 0.096± 0.006                         | 0.096± 0.006 | 0.098± 0.005 | 0.099± 0.007 | 0.104± 0.009 |

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(HAN300)

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| STUDY NO.: 0267<br>ANIMAL : RAT F344/DuC-j<br>UNIT : g/kg/day<br>REPORT TYPE : A1 104<br>SEX : MALE |                |              | HEMICAL INTAKE CHANGES<br>L ANIMALS | (SUMMARY)    |              |              | PAGE         | : 5 |
|-----------------------------------------------------------------------------------------------------|----------------|--------------|-------------------------------------|--------------|--------------|--------------|--------------|-----|
| Group Name                                                                                          | Administration | (weeks)      |                                     |              |              |              |              |     |
|                                                                                                     | 74             | 78           | 82                                  | 86           | 90           | 94           | 98           |     |
| Control                                                                                             | 0.000± 0.000   | 0.000± 0.000 | 0.000± 0.000                        | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 |     |
| 750 ppm                                                                                             | 0.030± 0.002   | 0.030± 0.003 | 0.030± 0.003                        | 0.030± 0.004 | 0.031± 0.006 | 0.033± 0.007 | 0.033± 0.008 |     |
| 1500 ppm                                                                                            | 0.055± 0.004   | 0.055± 0.003 | 0.051± 0.009                        | 0.053± 0.008 | 0.054± 0.007 | 0.055± 0.008 | 0.055± 0.010 |     |
| 3000 ppm                                                                                            | 0.104± 0.007   | 0.102± 0.007 | 0.099± 0.012                        | 0.099± 0.018 | 0.105± 0.015 | 0.107± 0.018 | 0.113± 0.017 |     |

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| STUDY NO.: 0267<br>ANIMAL : RAT F344/DuCrj<br>UNIT : g/kg/day<br>REPORT TYPE : A1 104<br>SEX : NALE |                             |              | CHEMICAL INTAKE CHANGES<br>ALL ANIMALS |      |         |
|-----------------------------------------------------------------------------------------------------|-----------------------------|--------------|----------------------------------------|------|---------|
| Group Name                                                                                          | Administration (week<br>102 | ks)<br>104   |                                        | PAGE | : 6<br> |
| Control                                                                                             | 0.000± 0.000 (              | 0.000± 0.000 |                                        |      |         |
| 750 ppm                                                                                             | 0.035± 0.012 0              | 0.035± 0.010 |                                        |      |         |
| 1500 ppm                                                                                            | 0.054± 0.007 0              | 0.058± 0.009 |                                        |      |         |
| 3000 ppm                                                                                            | 0.112± 0.023 0              | 0.121± 0.024 |                                        |      |         |

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(HAN300)

APPENDIX E 2

#### CHEMICAL INTAKE CHANGES : SUMMARY, RAT : FEMALE

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj UNIT : g/kg/day REPORT TYPE : A1 104 SEX : FEMALE			EMICAL INTAKE CHANGES L ANIMALS	(SUMMARY)			PAGI	E: 7
Group Name	Administration 1	(weeks)2	3	4	5	6	7	
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	
750 ppm	0.085± 0.013	0.078± 0.010	0.071± 0.009	0.066± 0.007	0.063± 0.010	0.061± 0.010	0.058± 0.005	
1500 ppm	0.142± 0.010	0.128± 0.010	0.118± 0.014	0.110± 0.010	0.104± 0.008	0.099± 0.009	0.099± 0.013	
3000 ppm	0.278± 0.070	0.247± 0.038	0.211± 0.015	0.204± 0.019	0.193± 0.018	0.187± 0.020	0.189± 0.041	

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STUDY NO.: 0267 ANIMAL : RAT F344/DuCrj UNIT : g/kg/day REPORT TYPE : A1 104 SEX : FEMALE			CHEMICAL INTAKE CHANGES LL ANIMALS	(SUMMARY)			PAGE	E: 8
Group Name		(weeks)						
	8	9	10	11	12	13	14	
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	
750 ppm	0.053± 0.007	0.054± 0.014	0.057± 0.021	0.056± 0.013	0.054± 0.013	0.061± 0.027	0.059± 0.021	
1500 ppm	0.090± 0.012	0.087± 0.008	0.091± 0.012	0.089± 0.007	0.085± 0.007	0.091± 0.025	0.091± 0.035	
3000 ppm	0.169± 0.038	0.151± 0.012	0.165± 0.012	0.162± 0.013	0.152± 0.013	0.159± 0.014	0.157± 0.016	

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STUDY NO.: 0267 ANIMAL : RAT F344/DuCrj UNIT : g/kg/day REPORT TYPE : A1 104 SEX : FEMALE			HEMICAL INTAKE CHANGES LL ANIMALS	(SUMMARY)			ΡΑ	GE: 9
Group Name	Administration 18	(weeks)22	26	30	34	38	42	
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	
750 ppm	0.049± 0.010	0.057± 0.024	0.058± 0.019	0.055± 0.019	0.053± 0.021	0.053± 0.019	0.046± 0.017	
1500 ppm	0.081± 0.014	0.083± 0.009	0.088± 0.012	0.082± 0.012	0.083± 0.014	0.081± 0.018	0.073± 0.006	
3000 ppm	0.143± 0.014	0.152± 0.021	0.161± 0.022	0.158± 0.031	0.156± 0.022	0.156± 0.031	0.150± 0.032	

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(HAN300)

STUDY NO.: 0267 ANIMAL : RAT F344/DLC-j UNIT : g/kg/day REPORT TYPE : A1 104 SEX : FEMALE			CHEMICAL INTAKE CHANGES ALL ANIMALS	(SUMMARY)			PAGE	E: 10
Group Name	Administration	(weeks)						
	46	50	54	58	62	66	70	
		· · · · · · · · · · · · · · · · · · ·				•••• •		
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	
750 ppm	0.047± 0.020	0.043± 0.008	0.046± 0.015	$0.040 \pm 0.011$	0.042± 0.010	0.041± 0.012	0.039± 0.006	
1500 ppm	0.073± 0.012	0.072± 0.013	$0.077 \pm 0.023$	0.075± 0.022	0.079± 0.024	0.079± 0.026	0.083± 0.026	
	0.0101 0.012	0.0721 0.010	0.0771 0.025	0.0701 0.022	0.0751 0.024	0.0751 0.025	0.0831 0.026	
3000 ppm	0.154± 0.040	0.158± 0.038	0.169± 0.055	0.166± 0.048	0.183± 0.051	$0.182 \pm 0.051$	0.190± 0.051	

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STUDY NO.: 0267 ANIMAL : RAT F344/DuCrj UNIT : g/kg/day REPORT TYPE : A1 104 SEX : FEMALE			EMICAL INTAKE CHANGES L ANIMALS	(SUMMARY)			PAGE :	11
Group Name	Administration	(weeks)				· · · · ·		
	74	78	82	86	90	94	98	
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	
750 ppm	0.039± 0.010	0.039± 0.010	0.038± 0.010	0.039± 0.010	0.041± 0.010	0.039± 0.012	0.040± 0.011	
1500 ppm	0.085± 0.031	0.089± 0.029	0.088± 0.032	0.092± 0.031	0.098± 0.037	0.104± 0.037	0.101± 0.032	
3000 ppm	0.191± 0.046	0.193± 0.042	0.198± 0.046	0.197± 0.051	0.228± 0.087	0.225± 0.064	0.224± 0.077	

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(HAN300)

| STUDY NO.: 0267<br>ANIMAL : RAT F344/DLC-j<br>UNIT : g/kg/day<br>REPORT TYPE : A1 104<br>SEX : FEMALE |                       | CHEMICAL INTAKE CHANGES (SU<br>ALL ANIMALS | MMARY) | PAGE: 12                               |
|-------------------------------------------------------------------------------------------------------|-----------------------|--------------------------------------------|--------|----------------------------------------|
| Group Name                                                                                            | Administration<br>102 | ueeks)<br>104                              | ·      | ······································ |
| Control                                                                                               | 0.000± 0.000          | 0.000± 0.000                               |        |                                        |
| 750 ppm                                                                                               | 0.040± 0.013          | 0.042± 0.014                               |        |                                        |
| 1500 ppm                                                                                              | 0.103± 0.033          | 0.103± 0.035                               |        |                                        |
| 3000 ppm                                                                                              | 0.217± 0.087          | 0.221± 0.062                               |        |                                        |

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(HAN300)

APPENDIX F 1

HEMATOLOGY : SUMMARY, RAT : MALE

| p Name   | NO. of<br>Animals | RED BLC<br>1 O <sup>6</sup> / | DOD CELL<br>µl | HEMOGLO<br>g⁄dl | DBIN  | НЕМАТОС<br>% | CRIT  | MCV<br>f L |       | MCH<br>Pg  | ····· | MCHC<br>g∕dl |     | PLATELE<br>1 0³∕µ |       |
|----------|-------------------|-------------------------------|----------------|-----------------|-------|--------------|-------|------------|-------|------------|-------|--------------|-----|-------------------|-------|
| Control  | 37                | 8.29±                         | 1.65           | 14.4±           | 2.9   | 44.1±        | 7.7   | 53.7±      | 3.9   | 17.4±      | 1.1   | 32.4±        | 2.1 | 883±              | 215   |
| 750 ppm  | 40                | 8.86±                         | 1.34           | 15.5±           | 2.0   | 46.9±        | 5.4   | 53.8±      | 8.0   | 17.7±      | 1.6   | 33.1±        | 1.2 | $824\pm$          | 158   |
| 1500 ppm | 41                | 9.28±                         | 1.81*          | 16.3±           | 2.6** | 49.0±        | 7.3** | 53.9±      | 6.9   | 17.8±      | 1.5   | 33.2±        | 1.5 | $736\pm$          | 166** |
| 3000 ppm | 46                | 10.69±                        | 1.74**         | 18.3±           | 2.6** | 54.9±        | 7.8** | 51.7±      | 2.7** | $17.2 \pm$ | 0.9*  | 33.3±        | 1.1 | 668±              | 128** |

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(HCL070)

| X : MALE |                   | TYPE : A1                    |               |           |                   |    |        |   |      |   |        |   |        |    | PAGE   | :: 2 |
|----------|-------------------|------------------------------|---------------|-----------|-------------------|----|--------|---|------|---|--------|---|--------|----|--------|------|
| DUD Name | NO. of<br>Animals | ₩BC<br>1 0 <sup>3</sup> ⁄ µℓ | Dit<br>N-BAND | fferentia | L WBC (9<br>N-SEG | 6) | EOSINO |   | BASO |   | MONO   |   | LYMPHO |    | OTHERS |      |
| Control  | 37                | 9.82± 24.41                  | 1±            | 1         | 52±               | 12 | 2±     | 1 | 0±   | 0 | 5±     | 2 | 36±    | 10 | 4±     | 16   |
| 750 ppm  | 40                | 7.87± 6.53                   | 1±            | 1         | $52\pm$           | 12 | 2±     | 1 | 0±   | 0 | 5±     | 2 | 36±    | 10 | 5±     | 17   |
| 1500 ppm | 41                | 7.56± 8.59                   | 1±            | 2         | 47±               | 12 | 2±     | 1 | 0±   | 0 | 5±     | 2 | 39±    | 10 | 6±     | 20*  |
| 3000 ppm | 46                | 7.36± 5.27                   | 1±            | 1         | 49±               | 11 | $2\pm$ | 1 | 0±   | 0 | $5\pm$ | 2 | 40±    | 9  | 3±     | 13*  |

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APPENDIX F 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

| up Name  | NO. of<br>Animals | RED BLC<br>1 O <sup>6</sup> / | 00D CELL<br>µl | HEMOGLO<br>g∕dl | BIN | HEMATOC<br>% | RIT | MCV<br>f Q     |      | MCH<br>Pg |     | MCHC<br>g ⁄dl |     | PLATELE<br>1 0 <sup>3</sup> /µ |     |
|----------|-------------------|-------------------------------|----------------|-----------------|-----|--------------|-----|----------------|------|-----------|-----|---------------|-----|--------------------------------|-----|
| Control  | 35                | 7,98±                         | 1.47           | 14.5±           | 2.7 | 43.4±        | 7.2 | 55.7±          | 9.3  | 18.3±     | 2.1 | 33.1±         | 1.7 | 666±                           | 176 |
| 750 ppm  | 41                | 7.93±                         | 1.40           | 14.5±           | 2.5 | 43.4±        | 6.2 | 56 <b>.</b> 2± | 10.0 | 18.5±     | 2.5 | 33.2±         | 2.0 | 683±                           | 139 |
| 1500 ppm | 40                | 7.88±                         | 1.24           | 14.6±           | 1.8 | 43.5±        | 4.7 | 56.0±          | 6.2  | 18.7±     | 1.6 | 33.5±         | 1.7 | 686±                           | 134 |
| 3000 ppm | 38                | 7.83±                         | 1,26           | 14.4±           | 2.1 | 43.3±        | 6.2 | 55.6±          | 4.2  | 18.5±     | 1.3 | 33.3±         | 1.1 | 670±                           | 155 |

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(HCL070)

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oup Name	NO. of Animals	WBC 1 0 <sup>3</sup> /µl	Dit N-BAND	fferentia	L WBC (9 N-SEG	6)	EOSINO		BASO		Mono		LYMPHO		OTHERS	
Control	35	5.47± 10.55	1±	1	48±	15	1±	1	0±	0	4±	2	$41\pm$	13	5±	
750 ppm	41	5.84± 12.77	1±	1	52±	13	1±	1	0±	0	4±	2	36±	12	4±	
1500 ppm	40	4.20± 5.83	1±	2	52±	11	2±	2	0±	0	5±	2	36±	11	4±	
3000 ppm	38	4.75± 9.80	1±	1	52±	13	1±	1	0±	0	$5\pm$	2	37±	11	4±	

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APPENDIX G 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

⊳ Name	NO. of Animals	TOTAL H g / dl		ALBUMIN g⁄dl		A/G RAT	10	T-BILI mg∕dl		GLUCOSE mg⁄dĺ		T-CHOLE mg∕dl	STEROL	TRIGLYC mg⁄dl	ERIDE
Control	37	6.6±	0.3	3.4±	0.2	1.0±	0.1	0.20±	0.05	$152\pm$	23	203±	53	178±	120
750 ppm	40	6.4±	0.3	$3.4\pm$	0.2	1.1±	0.2	0.22±	0.12	148±	22	172±	52	$136\pm$	82
1500 ppm	41	6.3±	0.3**	$3.5\pm$	0.2	1.2±	0.1**	0.26±	0.27	153±	18	$131\pm$	33**	94±	48**
3000 ppm	46	6.0±	0.3**	$3.5\pm$	0.2	1.4±	0.2**	0.20±	0.05	$147\pm$	19	80±	23**	48±	22**

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up Name	NO. of Animals	PHOSPHO mg/dl	LIPID	GOT IU∕ℓ		GPT IU∕Ø		LDH IU/9	2	ALP IU∕Q	2	G-GTP IU∕ℓ		CPK IU/1	
Control	37	277±	75	70±	49	33±	10	224±	290	159±	60	7±	3	91±	27
750 ppm	40	$236\pm$	73	80±	49	32±	12	207±	129	$144\pm$	46	8±	5	83±	19
1500 ppm	41	187±	44**	83±	44*	31±	12	209±	124	148±	52	8±	4	85±	21
3000 ppm	46	$125\pm$	27**	93±	27**	30±	8	204±	87	$142\pm$	46	6±	5*	98±	32

iup Name	NO. of Animals	UREA NI mg∕dl		CREATIN mg/dl	INE	SODIUM mEq/l		POTASSI mEq/		CHLORIDE mEq∕2		CALCIUM mg/dl	1	INORGAN mg/dl	IC PHOSPHORU
Control	37	22.4±	6.9	0.7±	0.2	$141\pm$	1	3.6±	0.4	105±	2	10.7±	0.4	4.0±	0.7
750 ppm	40	21.6±	5.7	0.7±	0.2	$141\pm$	1	3.6±	0.3	105±	1	10.6±	0.3	4.1±	0.7
1500 ppm	41	20.0±	2.5	0.6±	0.1**	$141\pm$	1	3.7±	0.3	105±	1	10.4±	0.3**	4.0±	0.6
3000 ppm	46	21.8±	2.8	0.6±	0.1**	141±	1	3.7±	0.3	105±	1	10.0±	0.3**	3.9±	0.7

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(HCL074)

APPENDIX G 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

STUDY NO. : 0267	
ANIMAL : RAT MEASURE. TIME :	
SEX : MALE	REPORT TYPE : A1
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URINALYSIS

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PAGE: 1

oup Name	NO. of Animals	рН 5.0	6.0	6.5	7.0	7.5	8.0	8.5 CHI	Protein - ± + 2+ 3+ 4+	CHI	Glucose - ± + 2+ 3+ 4+ CHI	Ketone body - ± + 2+ 3+ 4+ CHI	Bilirubin — + 2+ 3+ CHI
Control	38	0	1	4	8	16	8	1	0 0 0 0 7 31		38 0 0 0 0 0	37 1 0 0 0 0	38 0 0 0
750 ppm	41	0	1	2	5	18	14	1	0 0 0 0 14 27		41 0 0 0 0 0	39 2 0 0 0 0	40 1 0 0
1500 ppm	41	0	0	2	11	12	14	2	0 0 0 0 14 27		41 0 0 0 0 0	39 2 0 0 0 0	40 1 0 0
3000 ppm	46	0	0	4	9	13	19	1	0 0 0 0 32 14	**	46 0 0 0 0 0	39 7 0 0 0 0	46 0 0 0

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iroup Name	NO. of Animals	Occult blood — ± + 2+ 3+ CHI	Urobilinogen ± + 2+ 3+ 4+ CHI	
Control	38	37 1 0 0 0	38 0 0 0 0	
750 ppm	41	39 2 0 0 0	40 1 0 0 0	
1500 ppm	41	36 3 2 0 0	41 0 0 0 0	
3000 ppm	46	29 4 2 0 11 **	46 0 0 0 0	

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## APPENDIX H 1

URINALYSIS : SUMMARY, RAT : MALE

p Name	NO. of Animals	TOTAL F g⁄dl	PROTEIN	ALBUMIN g/dl		A/G RAT	10	T-BILI mg∕dℓ		GLUCOSE mg/dl		T-CHOLE mg∕dl	STEROL	TRIGLYC mg∕dl	ERIDE
Control	35	6.8±	0.6	3.8±	0.4	1.3±	0.2	0.53±	2.08	$150\pm$	18	$158\pm$	51	140±	107
750 ppm	41	6.6±	0.4	3.8±	0.4	1.4±	0.2	0.19±	0.08	$145\pm$	20	$133\pm$	49	$104\pm$	143
1500 ppm	40	6.4±	0.5*	3.9±	0.4	1.6±	0.2**	0.20±	0.13	143±	16	113±	32**	56±	49**
3000 ppm	38	6.1±	0.5**	3.9±	0.3	1.8±	0.2**	0.17±	0.02	$141\pm$	15	84±	18**	48±	43**

> Name	NO. of Animals	PHOSPHO mg⁄dl	LIPID	GOT IU/J	2	GPT IU∕ℓ		LDH IU/	2	ALP IU/S	2	G-GTP IU∕ℓ		CPK IU/Q	
Control	35	$265\pm$	80	$152\pm$	218	59±	44	251±	120	$130\pm$	137	4±	2	91±	34
750 ppm	41	225±	71	131±	76	$54\pm$	35	324±	499	$122\pm$	109*	5±	3	92±	41
1500 ppm	40	$199\pm$	52**	$161\pm$	267	39±	41	269±	213	106±	98**	$4\pm$	2	88±	30
3000 ppm	38	156±	36**	$134\pm$	237	$28\pm$	33**	$290\pm$	313	82±	42**	3±	1*	$120\pm$	60**

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oup Name	NO. of Animals	UREA NI mg/dl		CREATIN mg/dl	INE	SODIUM mEq/l		POTASSI mEq/		CHLORIDE mEq/l		CALCIUN mg∕dl		INORGAN mg∕dl	IIC PHOSPHORU
Control	35	16.3±	4.7	0.5±	0.1	140±	2	3.6±	0.3	104±	4	10.6±	0.5	3.7±	1.1
750 ppm	41	16.9±	5.7	0.5±	0.1	$140\pm$	1	3.6±	0.4	$105\pm$	2	10.4±	0.3	3.6±	0.9
1500 ppm	40	17.9±	4.8	0.5±	0.1	$140\pm$	2	3.7±	0.3	$105\pm$	2	10.4±	0.4	3.7±	1.0
3000 ppm	38	22.9±	7.2**	0.6±	0.1	140±	3	$3.7\pm$	0.5	104±	3	10.1±	0.5**	3.7±	0.8

### APPENDIX H 2

#### URINALYSIS : SUMMARY, RAT : FEMALE

roup Name	NO. of	pli							Protein	Glucose	Ketone body	Bilirubin	
	Animals	5.0	6.0	6.5	7.0	7.5	8.0	8.5 CHI	- ± + 2+ 3+ 4+ CHI	- ± + 2+ 3+ 4+ CHI	± + 2+ 3+ 4+ CHI	- + 2+ 3+ CHI	
Control	38	0	2	5	9	13	8	1	0 0 2 8 15 13	38 0 0 0 0 0	35 3 0 0 0 0	37 0 0 1	
750 ppm	41	0	3	2	6	13	16	1	0 0 0 4 16 21	41 0 0 0 0 0	39 1 1 0 0 0	41 0 0 0	
1500 ppm	42	0	5	4	9	8	16	0	0 0 0 3 20 19	42 0 0 0 0 0	40 2 0 0 0 0	41 0 1 0	
3000 ppm	39	0	2	6	11	14	6	0	0 0 2 2 12 23	39 0 0 0 0 0	36 3 0 0 0 0	39 0 0 0	
Significant	difference	; *:	: P ≦	0.05	5	** :	P≦	0.01	Test	of CHI SQUARE			

URINALYSIS

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj MEASURE. TIME : 1 SEX : FEMALE REPORT TYPE : A

oup Name	NO. of Animals	0ccult blood ± + 2+ 3+ CHI	Urobilinogen ± + 2+ 3+ 4+ CHI	
Control	38	36 2 0 0 0	37 0 1 0 0	
750 ppm	41	305600*	41 0 0 0 0	
1500 ppm	42	9 1 2 4 26 **	42 0 0 0 0	
3000 ppm	39	1 0 1 2 35 **	39 0 0 0 0	

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#### APPENDIX I 1

# GROSS FINDINGS : SUMMARY, RAT : MALE : ALL ANIMALS

### GROSS FINDINGS (SUMMARY) ALL ANIMALS (0-105W)

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#### STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

PAGE: 1

rgan	Findings	Group Name NO. of Animals 5	Contral 50 (%)	750 ppm 50 (%)	1500 ppm 50 (%)	3000 ppm 50 (%)
kin/app	nodule		0 ( 0)	3 (6)	2 ( 4)	1 ( 2)
ubcutis	jaundice		0 ( 0)	0 ( 0)	1 (2)	0 ( 0)
	mass		6 (12)	10 (20)	7 (14)	5 (10)
ung	red zone		1 (2)	0 ( 0)	1 ( 2)	1 ( 2)
	brown zone		0 ( 0)	0 ( 0)	1 (2)	0 ( 0)
	black zone		1 (2)	0 ( 0)	0 ( 0)	0 ( 0)
	nodule		2 ( 4)	2 ( 4)	0 ( 0)	0 ( 0)
.ymph node	enlarged .		1 (2)	0 ( 0)	0 ( 0)	0 ( 0)
pleen	enlarged		5 (10)	1 (2)	4 ( 8)	2 ( 4)
tongue	nodule		0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)
forestomach	rupture		1 (2)	0 ( 0)	0 ( 0)	0 ( 0)
	ulcer		0 ( 0)	1 (2)	0 ( 0)	0 ( 0)
stomach	nodule		0 ( 0)	0 ( 0)	0 ( 0)	1 (2)
	rupture		0 ( 0)	1 (2)	0 ( 0)	0 ( 0)
cecum	nocule		0 ( 0)	0 ( 0)	1 (2)	0 ( 0)
	cyst		0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)
	deformed		0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)
large intes	hemorrhage		0 ( 0)	0 ( 0)	0 ( 0)	1 (2)
	nodule		0 ( 0)	0 ( 0)	0 ( 0)	1 (2)
liver	nodule		1 (2)	0 ( 0)	0 ( 0)	1 ( 2)
	roush		1 ( 2)	2 ( 4)	1 (2)	1 (2)
	granular		0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)

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### GROSS FINDINGS (SUMMARY) ALL ANIMALS (0-105W)

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

-gan	Findings	Group Name NO. of Animals	Control 50 (%)	750 ppm 50 (%)	1500 ppm 50 (%)	3000 ppm 50 (%)
iver	herniation		2 (4)	1 (2)	2 ( 4)	0 ( 0)
idney	granular		31 (62)	21 (42)	6 (12)	3 (6)
in bladd	nodule		1 (2)	0 ( 0)	0 ( 0)	0 ( 0)
ituitary	enlarged		5 (10)	7 (14)	4 ( 8)	1 ( 2)
	red zone		1 (2)	1 (2)	0 ( 0)	3 (6)
	nodule		5 (10)	8 (16)	5 (10)	2 ( 4)
vroid	enlarged		1 (2)	1 ( 2)	1 ( 2)	2 ( 4)
	red zone		1 (2)	0 ( 0)	0 ( 0)	0 ( 0)
renal	enlarged		2 (4)	2 ( 4)	0 ( 0)	2 ( 4)
	cyst		0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)
stis	atrophic		4 (8)	2 ( 4)	2 ( 4)	2 ( 4)
	nodule		39 (78)	36 (72)	47 (94)	45 (90)
ep/cligl	nodule		3 (6)	0 ( 0)	0 ( 0)	1 ( 2)
vinal cord	red zone		1 (2)	0 ( 0)	0 ( 0)	0 ( 0)
<b>'</b> 0	white		3 (6)	4 ( 8)	4 (8)	3 (6)
mbal gl	nodule		0 ( 0)	1 (2)	2 ( 4)	0 ( 0)
.eura	nodule		0 ( 0)	0 ( 0)	0 ( 0)	1 (2)
ritoneum	nadule		1 (2)	1 ( 2)	2 ( 4)	1 (2)
dominal c	ascites		2 (4)	0 ( 0)	1 (2)	2 ( 4)
noracic ca	hemorrhage		1 (2)	0 ( 0)	0 ( 0)	0 ( 0)
her	tail:nodule		1 (2)	2 ( 4)	0 ( 0)	0 ( 0)
	ear:nodule		0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)

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APPENDIX I 2

GROSS FINDINGS : SUMMARY, RAT : MALE

DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

GROSS FINDINGS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W) ~

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ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

STUDY NO. : 0267

gan	Findings	Group Name Control NO. of Animals 11 (%)	750 ppm 9 (%)	1500 ppm 9 (%)	3000 ppm 4 (%)
in/app	nodule	0 ( 0)	1 (11)	1 (11)	0 ( 0)
boutis	jaundice	0 ( 0)	0 ( 0)	1 (11)	0 ( 0)
	mass	2 (18)	2 (22)	3 (33)	0 ( 0)
Pg	red zone	1 ( 9)	0 ( 0)	0 ( 0)	0 ( 0)
	nodule	2 (18)	0 ( 0)	0 ( 0)	0 ( 0)
nph node	enlarged	1 ( 9)	0 ( 0)	0 ( 0)	0 ( 0)
.een	enlarged	3 (27)	0 ( 0)	1 (11)	0 ( 0)
estomach	rupture	1 ( 9)	0 ( 0)	0 ( 0)	0 ( 0)
	ulcer	0 ( 0)	1 (11)	0 ( 0)	0 ( 0)
mach	rupture	0 ( 0)	1 (11)	0 ( 0)	0 ( 0)
90 intes	hemorrhage	0 ( 0)	0 ( 0)	0 ( 0)	1 (25)
er	nadule	1 ( 9)	0 ( 0)	0 ( 0)	0 ( 0)
	rough	1 ( 9)	0 ( 0)	1 (11)	0 ( 0)
iney	granular	3 (27)	3 (33)	0 ( 0)	0 ( 0)
in bladd	nodule	1 ( 9)	0 ( 0)	0 ( 0)	0 ( 0)
tuitary	enlarged	2 (18)	7 (78)	2 (22)	1 (25)
	nadule	2 (18)	0 ( 0)	0 ( 0)	0 ( 0)
roid	red zone	1 ( 9)	0 ( 0)	0 ( 0)	0 ( 0)
renal	enlarged	1 ( 9)	1 (11)	0 ( 0)	1 (25)
tis	atrophic	0 ( 0)	0 ( 0)	0 ( 0)	1 (25)
	nadule	4 (36)	3 (33)	7 (78)	1 (25)
o/cli gl	nodule	1 ( 9)	0 ( 0)	0 ( 0)	0 ( 0)

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

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### GROSS FINDINGS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

PAGE :	2
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Organ	Findines	Group Name Control 	750 ppm 9 (%)	1500 ppm 9 (%)	3000 ppm 4 (%)
spinal cord	red zone	1 ( 9)	0 ( 0)	0 ( 0)	0 ( 0)
еуе	white	0 ( 0)	1 (11)	2 (22)	0 ( 0)
Zymbal gl	nadule	0 ( 0)	0 ( 0)	2 (22)	0 ( 0)
pleura	nadule	0 ( 0)	0 ( 0)	0 ( 0)	1 (25)
peritaneum	nadule	0 ( 0)	1 (11)	1 (11)	0 ( 0)
abdominal c	ascites	1 (9)	0 ( 0)	0 ( 0)	0 ( 0)
thoracic ca	hemorrhage	1 ( 9)	0 ( 0)	0 ( 0)	0 ( 0)
other	tail:nodule	1 ( 9)	1 (11)	0 ( 0)	0 ( 0)

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### APPENDIX I 3

## GROSS FINDINGS : SUMMARY, RAT : MALE : SACRIFICED ANIMALS (2-YEAR STUDY)

### GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (105W)

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#### STUDY NO. : 0267 ANINAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

### PAGE: 1

Fgan	Findings	Group Name Control NO. of Animals 39 (%)	750 ppm 41 (%)	1500 ppm 41 (%)	3000 ppm 46 (%)
kin/app	nodule	0 ( 0)	2 ( 5)	1 (2)	1 (2)
ubcutis	mass	4 (10)	8 (20)	4 (10)	5 (11)
lung	red zone	0 ( 0)	0 ( 0)	1 (2)	1 ( 2)
	brawn zane	0 ( 0)	0 ( 0)	1 (2)	0 ( 0)
	black zone	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)
	nodule	0 ( 0)	2 (5)	0 ( 0)	0 ( 0)
spleen	enlarsed	2 ( 5)	1 ( 2)	3 (7)	2 (4)
tongue	nodule	0 ( 0)	0 ( 0)	1 (2)	0 ( 0)
stomach	nodule	0 ( 0)	0 ( 0)	0 ( 0)	1 (2)
ecum	nodule	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)
	cyst	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)
	deformed	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)
large intes	nodule	0 ( 0)	0 ( 0)	0 ( 0)	1 (2)
liver	nodule	0 ( 0)	0 ( 0)	0 ( 0)	1 (2)
	roush	0 ( 0)	2 (5)	0 ( 0)	1 (2)
	granular	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)
	herniation	2 ( 5)	1 ( 2)	2 (5)	0 ( 0)
kidney	sranular	28 (72)	18 (44)	6 (15)	3 (7)
pituitary	enlarged	3 ( 8)	0 ( 0)	2 (5)	0 ( 0)
	red zone	1 ( 3)	1 ( 2)	0 ( 0)	3 (7)
	nodule	3 ( 8)	8 (20)	5 (12)	2 (4)
thyroid	enlarged	1 ( 3)	1 (2)	1 (2)	2 (4)

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#### STUDY NO. : 0267 ANIMAL : RAT F344/DuGrj REPORT TYPE : A1 SEX : MALE

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### GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (105W)

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### PAGE: 2

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0rgan	Findings	Group Name NO. of Animals	39	Contral (%)	4		750 ppm (%)	 1500 ppm 41 (%)	4	3000 ppm (%)
adrenal	enlarged		1	(3)		1	(2)	0 ( 0)	:	(2)
	cyst		0	( 0)		0	( 0)	0 ( 0)	:	(2)
testis	atrophic		4	(10)		2	(5)	2 (5)		. (2)
	nodule		35	(90)	3	3	(80)	40 (98)	4	(96)
prep/cligl	nodule		2	(5)		0	( 0)	0 ( 0)		(2)
өуө	white		3	(8)		3	(7)	2 (5)	:	3 (7)
Zymbal gl	nodule		0	( 0)		1	(2)	0 ( 0)	1	) ( 0)
peritoneum	nodule		1	(3)		0	( 0)	1 (2)		(2)
abdominal c	ascites		1	(3)		0	( 0)	1 (2)	:	2 ( 4)
other	tail:nodule		0	( 0)		1	(2)	0 ( 0)	:	) ( 0)
	ear:nodule		0	( 0)		1	(2)	0 ( 0)		) ( 0)
			v	( )		•	( 2)	0 ( 0)		

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### APPENDIX I 4

## GROSS FINDINGS : SUMMARY, RAT : FEMALE : ALL ANIMALS (2-YEAR STUDY)

#### STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

### GROSS FINDINGS (SUMMARY) ALL ANIMALS (0-105W)

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PAGE: 3

-gan	Findings	Group Name Control NO. of Animals 50 (%)	750 ppm 50 (%)	1500 ppm 50 (%)	3000 ppm 50 (%)
cin/app	nodule	0 ( 0)	1 (2)	1 (2)	0 ( 0)
	scab	0 ( 0)	2 ( 4)	7 (14)	1 (2)
boutis	jaundice	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)
	mass	13 (26)	12 (24)	4 ( 8)	7 (14)
ung	red	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)
	white zone	0 ( 0)	1 (2)	2 ( 4)	4 (8)
ymph node	enlarged	0 ( 0)	0 ( 0)	1 ( 2)	1 ( 2)
nymus	enlarged	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)
oleen	enlarged	5 (10)	4 ( 8)	4 ( 8)	2 ( 4)
	atrophic	0 ( 0)	0 ( 0)	0 ( 0)	1 (2)
	black zone	0 ( 0)	0 ( 0)	1 (2)	0 ( 0)
	nodule	1 ( 2)	1 (2)	0 ( 0)	0 ( 0)
eart	white zone	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 4)
	red zone	0 ( 0)	1 (2)	0 ( 0)	0 ( 0)
prestomach	ulcer	0 ( 0)	1 (2)	0 ( 0)	0 ( 0)
l stomach	ulcer	1 (2)	1 ( 2)	0 ( 0)	0 ( 0)
tomach	ulcer	0 ( 0)	2 ( 4)	0 ( 0)	0 ( 0)
mall intes	nodule	0 ( 0)	1 ( 2)	0 ( 0)	1 ( 2)
iver	pale	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)
	white zone	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)
	nodule	1 (2)	1 (2)	1 ( 2)	1 ( 2)
	rough	2 ( 4)	1 ( 2)	1 (2)	0 ( 0)

#### STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

#### GROSS FINDINGS (SUMMARY) ALL ANIMALS (0-105W)

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PAGE: 4

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)rgan	Findings	Group Name Control NO. of Animals 50 (%)	750 ppm 50 (%)	1500 ppm 50 (%)	3000 ppm 50 (%)
liver	herniation	5 (10)	2 ( 4)	2 (4)	1 (2)
kidney	granular				
		4 ( 8)	0 ( 0)	2 ( 4)	0 ( 0)
	nodular	0 ( 0)	0 ( 0)	1 (2)	0 ( 0)
rin bladd	congestion	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)
	nodule	0 ( 0)	1 (2)	0 ( 0)	0 ( 0)
pituitary	enlarged	6 (12)	7 (14)	7 (14)	4 (8)
	red zone	2 ( 4)	6 (12)	1 ( 2)	5 (10)
	nodule	3 ( 6)	5 (10)	7 (14)	1 ( 2)
thyroid	enlarged	1 (2)	3 (6)	1 (2)	0 ( 0)
drenal	enlarged	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)
	granular	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)
ovary	enlarged	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)
	cyst	0 ( 0)	3 (6)	2 ( 4)	1 ( 2)
rterus	nodule	3 (6)	8 (16)	6 (12)	7 (14)
	cyst	0 ( 0)	1 ( 2)	1 ( 2)	2 ( 4)
vagina	nodule	0 ( 0)	2 ( 4)	0 ( 0)	1 ( 2)
rep/cligl	nodule	3 (6)	5 (10)	3 (6)	3 (6)
spinal cord	red zone	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)
Эуө	white	2 ( 4)	3 (6)	4 (8)	1 (2)
Kymbal gl	nodule	1 (2)	1 (2)	1 (2)	0 ( 0)
etroperit	nadule	0 ( 0)	1 (2)	0 ( 0)	0 ( 0)
bdominal c	ascites	1 (2)	1 ( 2)	0 ( 0)	0 ( 0)

(HPT080)

STUDY NO. : 0267 ANIMAL : RAT F344/DuC-j REPORT TYPE : A1 SEX : FEMALE	GROSS FINDINGS (SUMMARY) ALL ANIMALS (0-105W)			PAGE : 5
Organ Findings	Group Name Control NO. of Animals 50 (%)	750 ppm 50 (%)	1500 ppm 50 (%)	3000 maa 50 (%)
thoracic ca pleural fluid	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)
other forelimb:nodule	0 ( 0)	0 ( 0)	1 (2)	0 ( 0)
(HPT080)				BAIS 3

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APPENDIX I 5

GROSS FINDINGS : SUMMARY, RAT : FEMALE

DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

### GROSS FINDINGS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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Organ	Findings	Group Name NO. of Animals	Cantral 12 (%)	750 ppm 9 (%)	1500 ppm 8 (%)	3000 ppm 11 (%)
skin/app	scab		0 ( 0)	0 ( 0)	0 ( 0)	1 (9)
subcutis	mass		5 (42)	2 (22)	1 (13)	2 (18)
lung	red		0 ( 0)	1 (11)	0 ( 0)	0 ( 0)
	white zone		0 ( 0)	1 (11)	0 ( 0)	3 (27)
lymph node	enlarged		0 ( 0)	0 ( 0)	1 (13)	1 ( 9)
thymus	enlarged		0 ( 0)	0 ( 0)	0 ( 0)	1 ( 9)
spleen	enlarged		3 (25)	2 (22)	2 (25)	1 (9)
	atrophic		0 ( 0)	0 ( 0)	0 ( 0)	1 (9)
	black zone		0 (.0)	0 ( 0)	1 (13)	0 ( 0)
	nodule		1 (8)	1 (11)	0 ( 0)	0 ( 0)
heart	white zone		0 ( 0)	0 ( 0)	0 ( 0)	2 (18)
	red zone		0 ( 0)	1 (11)	0 ( 0)	0 ( 0)
forestomach	ulcer		0 ( 0)	1 (11)	0 ( 0)	0 ( 0)
gl stomach	ulcer		1 ( 8)	1 (11)	0 ( 0)	0 ( 0)
stomach	ulcer		0 ( 0)	1 (11)	0 ( 0)	0 ( 0)
liver	pale		0 ( 0)	1 (11)	0 ( 0)	0 ( 0)
	white zone		0 ( 0)	0 ( 0)	1 (13)	0 ( 0)
	nodule		0 ( 0)	0 ( 0)	0 ( 0)	1 (9)
	roush		2 (17)	1 (11)	0 ( 0)	0 ( 0)
	herniation		1 (8)	1 (11)	1 (13)	0 ( 0)
kidney	granular		1 (8)	0 ( 0)	0 ( 0)	0 ( 0)
	nodular		0 ( 0)	0 ( 0)	1 (13)	0 ( 0)

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PAGE: 3

### GROSS FINDINGS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

STUDY NO. : 0267 ANIMAL : RAT F344/DLC-j REPORT TYPE : A1 SEX : FEMALE

rgan	Findings	Group Name Control NO. of Animals 12 (%)	750 ppm 9 (%)	1500 ppm 8 (%)	3000 ppm 11 (%)
					······
rin bladd	congestion	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 9)
	nodule	0 ( 0)	1 (11)	0 ( 0)	0 ( 0)
tuitary	enlarged	3 (25)	4 (44)	4 (50)	2 (18)
	red zane	0 ( 0)	0 ( 0)	0 ( 0)	1 (9)
	nadule	0 ( 0)	0 ( 0)	1 (13)	0 ( 0)
renal	granular	0 ( 0)	1 (11)	0 ( 0)	0 ( 0)
ary	enlarged	0 ( 0)	0 ( 0)	1 (13)	0 ( 0)
	cyst	0 ( 0)	1 (11)	0 ( 0)	0 ( 0)
terus	nodule	2 (17)	2 (22)	2 (25)	0 ( 0)
agina	nodule	0 ( 0)	2 (22)	0 ( 0)	0 ( 0)
ep/cligl	nodule	0 ( 0)	1 (11)	0 ( 0)	2 (18)
vinal cord	red zone	1 ( 8)	0 ( 0)	0 ( 0)	0 ( 0)
/e	white	1 ( 8)	0 ( 0)	1 (13)	0 ( 0)
mbal gl	nodule	0 ( 0)	1 (11)	1 (13)	0 ( 0)
dominal c	ascites	0 ( 0)	1 (11)	0 ( 0)	0 ( 0)
oracic ca	pleural fluid	0 ( 0)	1 (11)	0 ( 0)	0 ( 0)

(HPT080)

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BAIS 3

PAGE: 4

### APPENDIX I 6

# GROSS FINDINGS : SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS (2-YEAR STUDY)

roup Name	NO. of Animals	Body	Weight	ADRE	NALS	TEST	ES	HEAR	T	LUNG	S	KIDN	EYS	
Control	39	425±	42	0.182±	0.638	4.120±	1.494	1.235±	0.122	1.464±	0.216	2.826±	0.298	
750 ppm	41	431±	38	0.079±	0.029	4.305±	1.460	1.203±	0.123	1.560±	0.714	2.803±	0.257	
1500 ppm	41	403±	22	0.070±	0.009**	4.481±	1.100	1.112±	0.095**	1.461±	0.313	$2.629 \pm$	0.201**	
3000 ppm	46	$336\pm$	31**	0.085±	0.088**	4.685±	0.882	0.993±	0.080**	1.286±	0.149**	$2.444 \pm$	0.221**	

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STUDY NO. : 026 ANIMAL : RAT REPORT TYPE : A SEX : MALE UNIT: g	F344/DuCrj					WEIGHT:ABSC VAL ANIMALS	)LUTE (SUMMARY) (105W)			PAGE : 2
Group Name	NO. of Animals	SPL	.EEN	LIV	ER	BRA	IN	· ·		
Control	39	1.303±	0.976	12.310±	1.658	$2.057\pm$	0.040			
750 ppm	41	1.662±	2.467	$12.182 \pm$	1.894	2.052±	0.036			
1500 ppm	41	1.893±	3.189	11.181±	2.362**	2.040±	0.047			
3000 ppm	46	1.020±	1.037**	8.808±	1.202**	2.003±	0.053**			
Significant	difference;	*:P≦0.	.05 **	: P ≦ 0.01	<del></del>		Test of Dunnett		 	
(HCL040)			<u> </u>						 	BAIS 3

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APPENDIX J 1

### ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(2-YEAR STUDY)

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

### GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (105W)

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PAGE: 3

rgan	Findings	Group Name Control NO. of Animals 38 (%)	750 ppm 41 (%)	1500 ppm 42 (%)	3000 ppm 39 (%)
kin/app	nodule	0 ( 0)	1 (2)	1 (2)	0 ( 0)
	scab	0 ( 0)	2 ( 5)	7 (17)	0 ( 0)
ubcutis	jaundice	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)
	mass	8 (21)	10 (24)	3 (7)	5 (13)
ung	white zone	0 ( 0)	0 ( 0)	2 (5)	1 (3)
pleen	enlarged	2 ( 5)	2 (5)	2 ( 5)	1 (3)
tomach	ulcer	0 ( 0)	1 (2)	0 ( 0)	0 ( 0)
mall intes	nodule	0 ( 0)	1 (2)	0 ( 0)	1 (3)
iver	nodule	1 ( 3)	1 (2)	1 (2)	0 ( 0)
	rough	0 ( 0)	0 ( 0)	1 (2)	0 ( 0)
	herniation	4 (11)	1 (2)	1 ( 2)	1 (3)
idney	granular	3 ( 8)	0 ( 0)	2 ( 5)	0 ( 0)
ituitary	enlarsed	3 ( 8)	3 (7)	3 (7)	2 (5)
	red zone	2 (5)	6 (15)	1 ( 2)	4 (10)
	nodule	3 ( 8)	5 (12)	6 (14)	1 (3)
hyroid	enlarged	1 (3)	3 (7)	1 (2)	0 ( 0)
drenal	enlarged	1 (3)	0 ( 0)	0 ( 0)	0 ( 0)
Vary	cyst	0 ( 0)	2 (5)	2 (5)	1 (3)
iterus	nodule	1 (3)	6 (15)	4 (10)	7 (18)
	cyst	0 ( 0)	1 (2)	1 (2)	2 (5)
agina	nodule	0 ( 0)	0 ( 0)	0 ( 0)	1 (3)
rep/cligl	nadule	3 ( 8)	4 (10)	3 (7)	1 (3)

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### GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (105W)

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PAGE: 4

Organ	Findings	Group Name NO. of Animals	Control 38 (%)	750 ppm 41 (%)	1500 ppm 42 (%)	3000 ppm 39 (%)
еуе	white		1 (3)	3 (7)	3 (7)	1 (3)
Zymbal gi	nodule		1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)
retroperit	nadule		0 ( 0)	1 (2)	0 ( 0)	0 ( 0)
abdominal c	ascites		1 (3)	0 ( 0)	0 ( 0)	0 ( 0)
other	forelimb:nodule		0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)
(HPT080)		•		· · · · · · · · · · · · · · · · · · ·		BAI

### APPENDIX J 2

### ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

(2-YEAR STUDY)

up Name	NO. of Animals	Body (	Weight	ADREI	NALS	OVAR	IES	HEAR	r	LUNG	S	KIDN	EYS	
Contral	38	303±	36	0.077±	0.022	0.128±	0.035	0.931±	0.069	1.106±	0.308	1.921±	0.212	
750 ppm	41	277±	38**	0.074±	0.019	0.174±	0.330	0.901±	0.082	$1.044\pm$	0.127	1.883±	0.132	
1500 ppm	42	250±	41**	0.067±	0.011**	0.138±	0.069	0.834±	0.087**	1.020±	0.187*	1.820±	0.204*	
3000 ppm	39	203±	31**	0.066±	0.008**	0.121±	0.033	0.739±	0.072**	0.935±	0.092**	1.701±	0.119**	

DY NO. : 026 MAL : RAT ORT TYPE : A : FEMALE T: g	F344/DuCrj					WEIGHT:ABSO VAL ANIMALS	UTE (SUMMARY) 105W)	PAGE : 4
up Name	NO. of Animals	SPL	EEN	LIV	ER	BRA	N	
Control	38	1.712±	5.644	7.939±	2.702	1.869±	0.049	
750 ppm	41	0.769±	0.785	$7.141\pm$	0.940	1.857±	0.065	
1500 ppm	42	0.723±	0.832	6.539±	1.503**	1.845±	0.049	
3000 ppm	39	0.579±	0.986**	$5.537 \pm$	0.724**	.1.808±	0.055**	

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### APPENDIX K 1

## ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(2-YEAR STUDY)

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS (105W)

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PAGE : 1

oup Name	NO. of Animals		Weight (g)	ADRENALS	TESTES	HEART	LUNGS	KIDNEYS
Control	39	425±	42	0.043± 0.148	0.967± 0.336	0.293± 0.037	0.349± 0.077	0.672± 0.101
750 ppm	41	$431\pm$	38	0.018± 0.007	1.006± 0.351	0.281± 0.042	0.368± 0.200	0.654± 0.079
1500 ppm	41	403±	22	0.017± 0.002	1.113± 0.270	0.277± 0.025	0.362± 0.074	0.654± 0.056
3000 ppm	46	336±	31**	0.025± 0.022	1.406± 0.289**	0.297± 0.022	0.384± 0.044**	0.731± 0.069**

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(HCL042)

BAIS 3

oup Name	NO. of Animals	SPLEEN	LIVER	BRAIN	
Control	39	0.317± 0.287	2.917± 0.459	0.489± 0.051	
750 ppm	41	0.401± 0.661	2.838± 0.462	0.479± 0.039	
1500 ppm	41	0.467± 0.769	2.776± 0.569**	0.507± 0.025	
3000 ppm	46	0.302± 0.303	2.622± 0.270**	0.601± 0.053**	

### APPENDIX K 2

### ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(2-YEAR STUDY)

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE UNIT: %

#### ORGAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS (105W)

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PAGE : 3

oup Name	NO. of Animals	Body	Weight (g)	ADRENALS	OVARIES	HEART	LUNGS	KIDNEYS	
Control	38	303±	36	0.025± 0.007	0.042± 0.010	0.314± 0.063	0.379± 0.173	0.649± 0.151	<u> </u>
750 ppm	41	277±	38**	0.028± 0.009	0.066± 0.135	0.331± 0.054	0.386± 0.094	0.693± 0.121	
1500 ppm	42	250±	41**	0.028± 0.005	0.056± 0.025**	0.340± 0.052	0.420± 0.118**	0.742± 0.112**	
3000 ppm	39	203±	31**	0.033± 0.007**	0.060± 0.015**	0.368± 0.045**	0.469± 0.076**	0.853± 0.128**	

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BAIS 3

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE UNIT: %

#### ORGAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS (105W)

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PAGE: 4 . Υ. NO. of Group Name SPLEEN BRAIN LIVER Animals Control 38  $0.728 \pm 2.599$  $2.700 \pm 1.349$  $0.628 \pm 0.095$ 750 ppm 41  $0.295 \pm 0.360$  $2.605 \pm 0.393$  $0.684 \pm 0.116$ 1500 ppm 42  $0.307 \pm 0.390$  $2.646 \pm 0.569$ 0.756± 0.110\*\* 3000 ppm 39  $0.283 \pm 0.465$ 2.751± 0.343\*\* 0.908± 0.134\*\* Significant difference ;  $*: P \leq 0.05$ \*\* : P ≦ 0.01 Test of Dunnett

(HCL042)

BAIS 3

### APPENDIX L 1

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

RAT : MALE : ALL ANIMALS

(2-YEAR STUDY)

REPORT TYPE :	RAT F344/DuC-j A1 MALE	ALL ANTA	ALS (0-105W)			PAGE :
0rgan	Findings	Group Name No. of Animals on Study Grade <u>1</u> (%)	Control 50 <u>2 3 4</u> (%) (%) (%)	$\begin{array}{c} 750 \text{ ppm} \\ 50 \\ \hline (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$	$\begin{array}{c} 1500 \text{ ppm} \\ 50 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$	$\begin{array}{c} 3000 \text{ ppm} \\ 50 \\ \hline 1 & 2 & 3 & 4 \\ \hline \% & (\%) & (\%) & (\%) \end{array}$
[Integumentary	' system/appandage]					
subcutis	abscess	0 ( 0)	<50> 1 0 0 ( 2) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	epidermal cyst	0 ( 0)	2 0 0 ( 4) ( 0) ( 0)	0 2 0 0 ( 0) ( 4) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
[Respiratory :	system]					
nasal cavit	mineralization	1 ( 2)	<50> 0 0 0 ( 0) ( 0) ( 0)	<50> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	inflammation	6 (12)	1 0 0 (2)(0)(0)	4 1 0 0 (8)(2)(0)(0)	2 0 0 0 ( 4) ( 0) ( 0) ( 0)	0 0 0 0 * (0)(0)(0)(0)
	inflammatory polyp	0 ( 0)	0 0 0 ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 2) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	goblet cell hyperplasia	3 ( 6)	0 0 0 ( 0) ( 0) ( 0)	4 0 0 0 (8)(0)(0)(0)	4 0 0 0 (8)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)
	eosinophilic change:olfactory epithe		1 0 0 (2)(0)(0)	40 2 0 0 (80)(4)(0)(0)	41 1 0 0 (82) (2) (0) (0)	43 1 0 0 (86)(2)(0)(0)

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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

#### STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

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

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PAGE: 2

		Group Name No. of Animals on Study		Control 50		_	7 5				50					3000 pp 50	
D <b>r</b> gan	Findings	Grade <u>1</u> (%)	2 (%)	3 (%)	<u>4</u> (%)	<u>1</u> (%)	2 (%)	3 (%)	<u>4</u> (%)	1(%)	2 (%)	3 (%)	<u>4</u> (%)	1 (%)	2 (%)	3 (%)	4(%
[Respiratory :	system]																
nasal cavit	eosinophilic change:respiratory epit	nelium 11 (22)	0	50> 0 ( 0)	0 ( 0)	1 ( 2)	<5 0 ( 0)	0	0 ** ( 0)	1 (2)	<5( 0 ( 0)	0	0 ** 0)	8 (16)			0
	inflammation:foreign body	9 (18)	1 (2)	0 ( 0)	0 ( 0)	20 ( 40)	3 (6)	0	0* (0)	13 (26)	0 ( 0)	0 ( 0) (	0 0)	10 ( 20)	1 ) ( 2)	0	0
	respiratory metaplasia:olfactory epi		0 ( 0)	0 ( 0)	0 ( 0)	7 (14)	0 (0)	0 ( 0)	0 ( 0)	5 (10)	0 ( 0)	0 ( 0) (	0 0)	2 ( 4)	0 ) ( 0)		0
	respiratory metaplasia:gland	23 ( 46)	0 ( 0)	0 ( 0)	0 ( 0)	13 (26)	0 (0)	0	0 ( 0)	10 (20)	0 ( 0)	0 ( 0) (	0 * 0)	25 (50)	0 ) ( 0)	0 ( 0)	0
	squamous cell metaplasia:respiratory		0 ( 0)	0 ( 0)	0 ( 0)	3 (6)	0 (0)	0	0 ( 0)	4 (8)	1 (2)	0 ( 0) (	0 0)	1 ( 2)	0 ) ( 0)	0 ( 0)	0
	hyperplasia:respiratory epithelium	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 (0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 (2)(	0 0)	0 ( 0)	0 ) ( 0)	0	0
nasopharynx	mineralization	0 ( 0)	0	50> 0 (0)	0	0 ( 0)	0	0> 0 ( 0)	0 ( 0)	0	<5( 0 ( 0)	0	0 0)	2 ( 4			0
	inflammation	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0	0 ( 0)	0	0 ( 0)	0 ( 0) (	0 0)	1 ( 2)	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 ; \*:  $P \le 0.05$  \*\* :  $P \le 0.01$  Test of Chi Square

)rgan	Findings	Group Name         Control           No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%)	$ \begin{array}{c} 750 \text{ ppm} \\ 50 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $	$ \begin{array}{c} 1500 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$ \begin{array}{c} 3000 \text{ ppm} \\ 50 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $
Respiratory	system]				
ing	congestion	<50> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<50> 7 0 0 0 (14) (0) (0) (0)	<50> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<50> 2 0 0 0 ( 4) ( 0) ( 0) ( 0)
	hemorrhage	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	edema	1 0 0 0 (2)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	inflammation	1 0 0 0 (2)(0)(0)(0)(0)	2 0 0 0 (4)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	3 0 0 0 (6)(0)(0)(0)
	osseous metaplasia	2 0 0 0 ( 4) ( 0) ( 0) ( 0)	0 0 0 0 (0)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	accumulation of foamy cells	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)(0)	4 0 0 0 (8)(0)(0)(0)	3 0 0 0 (6)(0)(0)(0)
	bronchiolar-alveolar cell hyperplasia	3     1     0     0       (6)     (2)     (0)     (0)	1 0 0 0 (2)(0)(0)(0)	4 0 0 0 (8)(0)(0)(0)	1 1 0 0 (2)(2)(0)(0)
Hematopoiet	c system]				
one marrow	congestion	<50> 2 0 0 0 ( 4) ( 0) ( 0) ( 0)	<50> 2 0 0 0 ( 4) ( 0) ( 0) ( 0)	<50> 3 0 0 0 ( 6) ( 0) ( 0) ( 0)	<50> 2 0 0 0 ( 4) ( 0) ( 0) ( 0)

(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) ALL ANIMALS (0-105W)

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

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'gan	Findings	Group Name Control No. of Animals on Study 50 Grade <u>1 2 3 4</u> (%) (%) (%) (%)	$ \begin{array}{c} 750 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$ \begin{array}{c} 1500 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ \hline (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$ \begin{array}{c} 3000 \text{ ppm} \\ 50 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $
ematopoietio	c system]				
ine martow	hemorrhage	<50> 6 0 0 0 · (12) (0) (0) (0)	<50> 6 0 0 0 (12) (0) (0) (0)	<50> 2 0 0 0 ( 4) ( 0) ( 0) ( 0)	<50> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)
	granulation	2 0 0 0 ( 4) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 0 0 0 (4)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)
	decreased hematopoiesis	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)(0)
	erythropoiesis:increased	10 0 0 0 (20) (0) (0) (0)	4 0 0 0 (8)(0)(0)(0)	2 0 0 0 * (4)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)
nph nade	lymphadenitis	<50> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
leen	atrophy	<50> 2 0 0 0 ( 4) ( 0) ( 0) ( 0)	<49> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 2 0 0 0 ( 4) ( 0) ( 0) ( 0)	<50> 1 0 0 0 (2) (0) (0) (0)
	congestion	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 (2)(0)(0)(0)

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

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ALL ANIMALS (0-105W)

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

<a>>

b : Number of animals with lesion c : b / a \* 100 b

(c)

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

(HPT150)

STUDY NO. : 0267

ANIMAL : RAT F344/DuCrj

|            |                              | Group Name Control<br>No. of Animals on Study 50<br>Grade <u>1 2 3 4</u> | 750 ppm<br>50<br>1 2 3 4                                         | 1500 ppm<br>50<br>1 2 3 4              | 3000 ppm<br>50<br>1 2 3 4                            |
|------------|------------------------------|--------------------------------------------------------------------------|------------------------------------------------------------------|----------------------------------------|------------------------------------------------------|
| 0rgan      | Findings                     | (%) (%) (%)                                                              | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$ | (%) (%) (%) (%)                        | (%) (%) (%) (%)                                      |
| lematopoie | tic system]                  |                                                                          |                                                                  |                                        |                                                      |
| spleen     | hemorrhage                   | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | <49><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                           | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)               |
|            | deposit of hemosiderin       | 31 2 0 0<br>(62)(4)(0)(0)                                                | 45 0 0 0 **<br>(92) (0) (0) (0)                                  | 40 1 0 0<br>(80) (2) (0) (0)           | 30 0 0 0<br>(60)(0)(0)(0)                            |
|            | granulation                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | 1 0 0 0<br>(2)(0)(0)(0)(0)             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
|            | fibrosis                     | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$                    | 2 0 0 0<br>(4)(0)(0)(0)                                          | 4 0 0 0<br>(8)(0)(0)(0)                | 1 0 0 0<br>(2)(0)(0)(0)                              |
|            | extramedullary hematopoiesis | 16 3 0 0<br>(32)(6)(0)(0)                                                | 9 2 0 0<br>(18) (4) (0) (0)                                      | 7 1 0 0*<br>(14)(2)(0)(0)              | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ |
|            | fatty metamorphosis          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                           | 1 0 0 0<br>(2)(0)(0)(0)                                          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
| Circulator | v system]                    |                                                                          |                                                                  |                                        |                                                      |
| eart       | thrombus                     | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                   | <50><br>3 0 0 0<br>(6)(0)(0)(0)                                  | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0) | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |

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| rgan         | Findings            | Group Name Control<br>No. of Animals on Study 50<br>Grade <u>1 2 3</u><br>(%) (%) (%) | $\begin{array}{c} & 750 \text{ ppm} \\ & 50 \\ \hline 4 \\ \hline (\%) & 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \\ \hline \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | 3000 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|--------------|---------------------|---------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|-----------------------------------------------------|
| Circulatory  | system]             |                                                                                       |                                                                                                                                                   |                                                       |                                                     |
| eart         | mineralization      | <50><br>0 1 0<br>( 0) ( 2) ( 0)                                                       | <50><br>0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0) ( 0)                                                                                                     | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |
|              | myocardial fibrosis | 30 2 0<br>(60)(4)(0)                                                                  | 0 32 2 0 0<br>( 0) ( 64) ( 4) ( 0) ( 0)                                                                                                           | 27 0 0 0<br>(54)(0)(0)(0)                             | 28 1 0 0<br>(56)(2)(0)(0)                           |
| rtery/aort   | arteritis           | <50><br>0 0 0<br>( 0) ( 0) ( 0)                                                       | <pre></pre>                                                                                                                                       | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |
| Digestive sy | /stem]              |                                                                                       |                                                                                                                                                   |                                                       |                                                     |
| oeth         | inflammation        | <50><br>4 0 0<br>( 8) ( 0) ( 0)                                                       | <pre></pre>                                                                                                                                       | <50><br>6 0 0 0<br>(12) (0) (0) (0)                   | <50><br>9 0 0 0<br>(18) (0) (0) (0)                 |
| tomach       | mineralization      | <50><br>0 0 1<br>( 0) ( 0) ( 2)                                                       | <50><br>0 1 0 0 0<br>( 0) ( 2) ( 0) ( 0) ( 0)                                                                                                     | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0               |
|              | ulcer:forestomach   | 0 0 0<br>( 0) ( 0) ( 0)                                                               | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                                              | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                        | 0 1 0 0<br>(0)(2)(0)(0                              |

(HPT150)

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

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

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| 0rgan         | Findings                     | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | Cantrol<br>50<br><u>2 3 4</u><br>(%) (%) (%) | 750 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$                           | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
|---------------|------------------------------|----------------------------------------------------------------|----------------------------------------------|----------------------------------------------------|---------------------------------------------------------------------------------|-------------------------------------------------------|
| [Digestive sy | stem]                        |                                                                |                                              |                                                    |                                                                                 |                                                       |
| stomach       | hyperplasia:forestomach      | 0<br>( 0)                                                      | <50><br>1 0 0<br>( 2) ( 0) ( 0)              | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)             | $\begin{array}{c} <50>\\ 1 & 1 & 0 & 0\\ ( 2) & ( 2) & ( 0) & ( 0) \end{array}$ | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
|               | erosion:glandular stomach    | 2<br>( 4)                                                      | 0 0 0<br>( 0) ( 0) ( 0)                      | 1 1 0 0<br>(2)(2)(0)(0)                            | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                            | 2 0 0 0<br>(4) (0) (0) (0)                            |
|               | ulcer:glandular stomach      | 0<br>( 0)                                                      | 1 0 0<br>(2)(0)(0)                           | 1 0 1 0<br>(2)(0)(2)(0)                            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |
|               | hemorrhage:glandular stomach | 0<br>( 0)                                                      | 0 0 0<br>( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                  | 1 0 0 0<br>(2)(0)(0)(0)                               |
| large intes   | mineralization               | 3<br>( 6)                                                      | <50><br>1 0 0<br>( 2) ( 0) ( 0)              | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0)             | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                          | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
|               | arteritis                    | 0<br>( 0)                                                      | 0 0 0<br>( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                  | 0 0 1 0<br>( 0) ( 0) ( 2) ( 0)                        |
|               | . Lymphangiectasia           | 0<br>( 0)                                                      | 0 0 0<br>( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                  | 1 0 0 0<br>(2)(0)(0)(0)                               |
| liver         | herniation                   | 2<br>( 4)                                                      | <50><br>0 0 0<br>( 0) ( 0) ( 0)              | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)             | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                                          | <50><br>0 0 0 0<br>( 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

STUDY NO. : 0267

REPORT TYPE : A1

SEX

ANIMAL : RAT F344/DuCrj

: MALE

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

(HPT150)

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

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PAGE: 7

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| : RAT F344/DuCrj<br>: A1<br>: MALE | ALL ANIMALS (0-105W)                                                                                                                                                                                      |                                                                                                                  |                                                       | PAGE : 8                                               |
|------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|--------------------------------------------------------|
| Findings                           | Group Name         Control           No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%)                         | $\begin{array}{c} 750 \text{ ppm} \\ 50 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  |
| system]                            |                                                                                                                                                                                                           |                                                                                                                  |                                                       |                                                        |
| hemorrhage                         | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                                    | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                 |
| peliasis-like lesian               | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                                                                                                      | 6 0 0 0<br>(12) (0) (0) (0)                                                                                      | 6 0 0 0<br>(12) (0) (0) (0)                           | 3 0 0 0<br>(6)(0)(0)(0)                                |
| necrosis:central                   | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                                                                                                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                         |
| necrosis:focal                     | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                                                                                                      | 1 0 0 0<br>(2)(0)(0)(0)                                                                                          | 1 0 0 0<br>(2)(0)(0)(0)                               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                         |
| fatty change                       | 4 0 0 0<br>( 8) ( 0) ( 0) ( 0)                                                                                                                                                                            | 2 0 2 0<br>( 4) ( 0) ( 4) ( 0)                                                                                   | 4 0 0 0<br>(8)(0)(0)(0)                               | 1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                         |
| fatty change:peripheral            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                                            | 1 0 0 0<br>(2)(0)(0)(0)                                                                                          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                         |
| inflammatory infiltration          | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                                                                                                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                         |
| granulation                        | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                                                                                                      | 14 2 0 0<br>(28) (4) (0) (0)                                                                                     | 9 1 0 0<br>(18) (2) (0) (0)                           | 3 1 0 0 *<br>(6)(2)(0)(0)                              |
|                                    | : A1<br>: MALE<br>Findings<br>system]<br>hemorrhage<br>peliosis-like lesion<br>necrosis:central<br>necrosis:focal<br>fatty change<br>fatty change<br>fatty change:peripheral<br>inflammatory infiltration | $\begin{array}{c ccccccccccccccccccccccccccccccccccc$                                                            | $\begin{array}{c ccccccccccccccccccccccccccccccccccc$ | $\begin{array}{c c c c c c c c c c c c c c c c c c c $ |

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

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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

STUDY NO. : 0267

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

| )rgan       | Findings               | Group Name         Control           No. of Animals on Study         50           Grade         1         2         3         4 | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{c} 1500 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $\begin{array}{c} 3000 \text{ ppm} \\ 50 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array}$ |
|-------------|------------------------|---------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------|
| Digestive s | system]                |                                                                                                                                 |                                                       |                                                                                                                   |                                                                                                           |
| iver.       | clear cell focus       | <50><br>12 0 0 0<br>(24) (0) (0) (0)                                                                                            | <50><br>9 0 0 0<br>(18) (0) (0) (0)                   | <50><br>8 1 0 0<br>(16) (2) (0) (0)                                                                               | <50><br>3 0 0 0 *<br>( 6) ( 0) ( 0) ( 0)                                                                  |
|             | acidophilic cell focus | 9 0 0 0<br>(18) (0) (0) (0)                                                                                                     | 7 0 0 0<br>(14) (0) (0) (0)                           | 1 0 0 0 *<br>(2)(0)(0)(0)                                                                                         | 3 0 0 0<br>(6)(0)(0)(0)(0)                                                                                |
|             | basophilic cell focus  | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                            | 7 0 0 0<br>(14) (0) (0) (0)                           | 5 0 0 0<br>(10) (0) (0) (0)                                                                                       | 7 0 0 0<br>(14) (0) (0) (0)                                                                               |
|             | vacuolated cell focus  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                  | 4 0 0 0<br>(8)(0)(0)(0)                               | 4 0 0 0<br>(8)(0)(0)(0)                                                                                           | 4 0 0 0<br>( 8) ( 0) ( 0) ( 0)                                                                            |
|             | mixed cell focus       | 1 0 0 0<br>(2)(0)(0)(0)                                                                                                         | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                        | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                                                                                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                            |
|             | spongiosis hepatis     | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                           | 11 0 0 0<br>(22) ( 0) ( 0) ( 0)                       | 9 1 0 0<br>(18) (2) (0) (0)                                                                                       | 2 0 0 0 *<br>( 4) ( 0) ( 0) ( 0)                                                                          |
|             | bile duct hyperplasia  | 43 6 0 0<br>(86) (12) (0) (0)                                                                                                   | 39 10 0 0<br>(78) (20) (0) (0)                        | 44 5 0 0<br>(88) (10) (0) (0)                                                                                     | 45 2 0 0<br>(90)(4)(0)(0)                                                                                 |
| ancreas     | atrophy                | <50><br>5 0 0 0<br>(10) (0) (0) (0)                                                                                             | <50><br>11 2 0 0<br>(22) (4) (0) (0)                  | <50><br>13 0 0 0<br>(26) (0) (0) (0)                                                                              | <50><br>10 1 0 0<br>(20) (2) (0) (0)                                                                      |

1: Slight Grade 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

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

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

| STUDY NO. : 0267<br>ANIMAL : RAT F344/DuCrj<br>REPORT TYPE : A1<br>SEX : MALE |                        | HISTOLOGICAL FINDINGS :NON-NE<br>ALL ANIMALS (0-105W)                                       |                                                                                                                  | PAGE : 10                                                                                                                |                                                                                                                   |
|-------------------------------------------------------------------------------|------------------------|---------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|
| 0rgan                                                                         | Findings               | Group Name Control<br>No. of Animals on Study 50<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{c} 750 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $ \begin{array}{c} 1500 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $ \begin{array}{c} 3000 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
| [Urinary syst                                                                 | em]                    |                                                                                             |                                                                                                                  |                                                                                                                          |                                                                                                                   |
| kidney                                                                        | basophilic change      | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                      | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | <50><br>1 1 0 0<br>( 2) ( 2) ( 0) ( 0)                                                                            |
|                                                                               | deposit of hemosiderin | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                                        | 5 0 0 0<br>(10) (0) (0) (0)                                                                                      | 5 0 0 0<br>(10) (0) (0) (0)                                                                                              | 1 0 0 0<br>(2)(0)(0)(0)                                                                                           |
|                                                                               | eosinophilic body      | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                                        | 10 0 0 0<br>(20)(0)(0)(0)                                                                                        | 8 0 0 0<br>(16)(0)(0)(0)                                                                                                 | 8 1 0 0<br>(16) (2) (0) (0)                                                                                       |
|                                                                               | chronic nephropathy    | 0 14 31 3<br>( 0) ( 28) ( 62) ( 6)                                                          | 1 19 22 8<br>(2)(38)(44)(16)                                                                                     | 0 33 17 0 **<br>( 0) (66) (34) ( 0)                                                                                      | 5 38 5 0 **<br>(10) (76) (10) (0)                                                                                 |
|                                                                               | papillary necrosis     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                              | 1 0 0 0<br>(2)(0)(0)(0)                                                                                          | 9 0 0 0 **<br>(18) (0) (0) (0)                                                                                           | 23 1 0 0 **<br>(46)(2)(0)(0)                                                                                      |
|                                                                               | mineralization:peluis  | 2 0 0 0<br>(4)(0)(0)(0)                                                                     | 1 0 0 0<br>(2)(0)(0)(0)                                                                                          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                    |
|                                                                               | mineralization:cortex  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | 2 0 0 0<br>(4)(0)(0)(0)                                                                                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                    |
| urin bladd                                                                    | ulcer                  | <50><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                                                      | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                            |

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< 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

| STUDY NO. : 0267<br>ANIMAL : RAT F344/DuCrj<br>REPORT TYPE : A1<br>SEX : MALE |                        | HISTOLOGICAL FINDINGS :NON-NI<br>ALL ANIMALS (0-105W)                                       | HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)<br>ALL ANIMALS (0-105W)                                |                                                     | PAGE : 11                                           |  |
|-------------------------------------------------------------------------------|------------------------|---------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------|-----------------------------------------------------|-----------------------------------------------------|--|
| Organ                                                                         | Findings               | Group Name Control<br>No. of Animals on Study 50<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 750 \text{ ppm} \\ 50 \\ \hline 1 & 2 & 3 & 4 \\ \hline \% & (\%) & (\%) & (\%) \end{array}$ | 1500 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 3000 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |  |
| [Urinary syst                                                                 | em]                    |                                                                                             |                                                                                                                |                                                     |                                                     |  |
| urin bladd                                                                    | mineralization         | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                      | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                         | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |  |
| [Endocrine sy                                                                 | stem]                  |                                                                                             |                                                                                                                |                                                     |                                                     |  |
| pituitary                                                                     | angiectasis            | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                      | <50><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                                                                         | <50><br>1 0 1 0<br>( 2) ( 0) ( 2) ( 0)              | <50><br>1 1 0 0<br>( 2) ( 2) ( 0) ( 0)              |  |
|                                                                               | hemorrhage             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                 | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 1 0 1 0<br>(2)(0)(2)(0)                             |  |
|                                                                               | necrosis:focal         | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$                                       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                 | 1 0 0 0<br>(2)(0)(0)(0)                             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      |  |
|                                                                               | cyst                   | $\begin{pmatrix} 1 & 0 & 0 & 0 \\ ( & 2) & ( & 0) & ( & 0) & ( & 0) \end{pmatrix}$          | 4 0 0 0<br>(8)(0)(0)(0)                                                                                        | 3 0 0 0<br>(6)(0)(0)(0)                             | 3 0 0 0<br>(6)(0)(0)(0)                             |  |
|                                                                               | deposit of hemosiderin | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                                                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                 | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                      | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                      |  |
|                                                                               | hyperplasia            | 6 8 0 0<br>(12)(16)(0)(0)                                                                   | 12 3 0 0<br>(24)(6)(0)(0)                                                                                      | 6 5 1 0<br>(12)(10)(2)(0)                           | 8 3 1 0<br>(16) (6) (2) (0)                         |  |

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

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

b : Number of animals with lesion ь

c:b/a\*100 (c)

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

|                                   | ······································                                                                  |                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | PAGE :                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|-----------------------------------|---------------------------------------------------------------------------------------------------------|----------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Findings                          | Group Name<br>No. of Animals on Study<br>Grade <u>1</u> (%)                                             | Cantrol<br>50<br><u>2 3 4</u><br>(%) (%) (%) | $\begin{array}{c} 750 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ \hline (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 3000 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| tem]                              |                                                                                                         |                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Rathke pouch                      | 0<br>( 0)                                                                                               | <50><br>0 0 0<br>( 0) ( 0) ( 0)              | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| hemorrhage                        | 0<br>( 0)                                                                                               | <50><br>0 0 0<br>( 0) ( 0) ( 0)              | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| cyst                              | 0<br>( 0)                                                                                               | 0 0 0<br>( 0) ( 0) ( 0)                      | 1 0 0 0<br>(2)(0)(0)(0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 1 0 0 0<br>(2)(0)(0)(0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 1 0 0 0<br>(2)(0)(0)(0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| C-cell hyperplasia                | 4<br>( 8)                                                                                               | 0 0 0<br>( 0) ( 0) ( 0)                      | 4 0 0 0<br>(8)(0)(0)(0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 9 1 0 0<br>(18) (2) (0) (0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 3 1 0 0<br>(6)(2)(0)(0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| focal follicular cell hyperplasia | 1<br>( 2)                                                                                               | 0 0 0<br>(0)(0)(0)                           | 3 1 0 0<br>(6)(2)(0)(0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 3 0 0 0<br>(6)(0)(0)(0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 1 1 0 0<br>(2) (2) (0) (0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| islet cell hyperplasia            | 2<br>( 4)                                                                                               | <50><br>0 0 0<br>( 0) ( 0) ( 0)              | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| peliosis-like lesion              | 0<br>( 0)                                                                                               | <50><br>0 0 0<br>( 0) ( 0) ( 0)              | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|                                   | hemorrhage<br>cyst<br>C-cell hyperplasia<br>focal follicular cell hyperplasia<br>islet cell hyperplasia | <pre>( 0) hemorrhage</pre>                   | Rathke pouch       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       < | Rathke pouch       0       0       0       0       0       0       0       1       0       0       0       0         hemorrhage $\begin{pmatrix} 50 \\ 0 \end{pmatrix}$ $\begin{pmatrix} 0 \\ 0$ | Ratike pouch       0       0       0       0       0       0       1       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       0       < |

Grade 3 : Marked 1 : Slight 2 : Moderate 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 ; \*:  $P \le 0.05$  \*\* :  $P \le 0.01$  Test of Chi Square

STUDY NO. : 0267

REPORT TYPE : A1

ANIMAL : RAT F344/DuCrj

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BAIS3

| 0rgan                                       | Findings                                                                                                                             | Group Name         Control           No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | 750 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{c} 3000 \text{ ppm} \\ 50 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $ |
|---------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|-------------------------------------------------------|-------------------------------------------------------------------------------------------------------------|
| [Endocrine :                                | system]                                                                                                                              |                                                                                                                                                                                               |                                                    |                                                       |                                                                                                             |
| adrenal                                     | necrosis:focal                                                                                                                       | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                                                                                                                        | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)             | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                      |
|                                             | cyst                                                                                                                                 | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                                                                              |
|                                             | hyperplasia:cortical cell                                                                                                            | 1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                                                                                                                                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                                                                              |
|                                             | hyperplasia:medulla                                                                                                                  | 7 2 0 0<br>(14) (4) (0) (0)                                                                                                                                                                   | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                     | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                        | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                                                                              |
|                                             | focal fatty change:cortex                                                                                                            | 3 0 0 0<br>(6)(0)(0)(0)                                                                                                                                                                       | 6 1 0 0<br>(12) (2) (0) (0)                        | 3 0 0 0<br>(6)(0)(0)(0)                               | 1 1 0 0<br>(2)(2)(0)(0)                                                                                     |
|                                             | cortical vacuolation:diffuse                                                                                                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                                | 1 0 0 0<br>(2)(0)(0)(0)                            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                              |
| [Reproducti                                 | ve system]                                                                                                                           |                                                                                                                                                                                               |                                                    |                                                       |                                                                                                             |
| testis                                      | atrophy                                                                                                                              | <50><br>9 0 0 0<br>(18) (0) (0) (0)                                                                                                                                                           | <50><br>1 0 0 0 *<br>( 2) ( 0) ( 0) ( 0)           | <50><br>5 0 0 0<br>(10) (0) (0) (0)                   | <50><br>3 0 0 0<br>( 6) ( 0) ( 0) ( 0)                                                                      |
| Grade<br>< a ><br>b<br>( c )<br>Significant | 1: Slight2: Moderatea: Number of animals examined at theb: Number of animals with lesionc: b / a * 100c difference; $*: P \leq 0.05$ |                                                                                                                                                                                               |                                                    |                                                       |                                                                                                             |

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

STUDY NO. : 0267

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

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(HPT150)

| rgan          | Findings                      | Group Name Control<br>No. of Animals on Study 50<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 750 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ | $\begin{array}{cccc} 1500 \text{ ppm} \\ 50 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | 3000 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|---------------|-------------------------------|---------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------|
| Reproductive  | system]                       |                                                                                             |                                                                                                                       |                                                                                                                      |                                                     |
| restis        | mineralization                | <50><br>6 0 0 0<br>(12) (0) (0) (0)                                                         | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                                                | <50><br>3 0 0 0<br>( 6) ( 0) ( 0) ( 0)                                                                               | <50><br>8 0 0 0<br>(16) (0) (0) (0)                 |
|               | interstitial cell hyperplasia | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                              | 2 0 0 0<br>(4)(0)(0)(0)                                                                                               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      |
| rostate       | granulation                   | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                      | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                               | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)              |
|               | hyperplasia                   | 8 5 0 0<br>(16)(10)(0)(0)                                                                   | 4 0 0 0 *<br>(8)(0)(0)(0)                                                                                             | 8 2 0 0<br>(16)(4)(0)(0)                                                                                             | 4 1 0 0<br>( 8) ( 2) ( 0) ( 0)                      |
| nammary gl    | galactocele                   | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                                                      | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                               | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0)              |
| prep/cligl    | inflammation                  | <50><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                                                      | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                               | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |
| [Special sens | e organs/appandage]           |                                                                                             |                                                                                                                       |                                                                                                                      |                                                     |
| эуө           | cataract                      | <50><br>3 0 0 0<br>( 6) ( 0) ( 0) ( 0)                                                      | <50><br>4 0 0 0<br>( 8) ( 0) ( 0) ( 0)                                                                                | <50><br>3 0 0 0<br>( 6) ( 0) ( 0) ( 0)                                                                               | <50><br>2 1 0 0<br>( 4) ( 2) ( 0) ( 0)              |

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) ALL ANIMALS (0-105W)

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

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

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Organ	Findings	Group Name Control No. of Animals on Study 50 Grade <u>1 2 3</u> (%) (%) (%)	$\begin{array}{c} 750 \text{ ppm} \\ 50 \\ \hline (\%) \hline (\%) \\ \hline (\%) $	$ \begin{array}{c} 1500 \text{ ppm} \\ 50 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $	$\begin{array}{c} 3000 \text{ ppm} \\ 50 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$
Special seps	e organs/appandage]				· · · · · · · · · · · · · · · · · · ·
уө	retinal atrophy	<50> 1 3 0 ( 2) ( 6) ( 0) (	<pre></pre>	<50> 2 1 1 0 ( 4) ( 2) ( 2) ( 0)	<50> 1 2 0 0 ( 2) ( 4) ( 0) ( 0)
	keratitis	2 1 0 ( 4) ( 2) ( 0) (	0 0 0 0 0 0) ( 0) ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 2) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	degeneration:cornea	7 0 0 (14) (0) (0) (	0 1 0 0 0 0) ( 2) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)	4 0 0 0 (8)(0)(0)(0)
	vascularization:cornea	1 0 0 (2)(0)(0)(	0 1 0 0 0 0) ( 2) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
arder gl	granulation	<50> 0 0 0 ( 0) ( 0) ( 0) (	<pre> &lt;50&gt; 0 0 0 0 0 0) ( 0) ( 0) ( 0) ( 0)</pre>	<50> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
nasolaer d	inflammation	<50> 1 0 0 ( 2) ( 0) ( 0) (	<50> 0 0 0 0 0 0) ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
[Musculoskele	vtal system]				
one	osteosclerosis	<50> 0 0 0 ( 0) ( 0) ( 0) (	<pre> &lt;50&gt; 0 1 0 0 0 0) ( 2) ( 0) ( 0) ( 0)</pre>	<50> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)

a : Number of animals examined at the site b : Number of animals with lesion b

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

## APPENDIX L 2

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

RAT : MALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

)rgan	N	roup Name Control o. of Animals on Study 11 rade <u>1 2 3 4</u> (%) (%) (%) (%)	$\begin{array}{c} 750 \text{ ppm} \\ 9 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$	$ \begin{array}{c} 1500 \text{ ppm} \\ 9 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$\begin{array}{c} 3000 \text{ ppm} \\ 4 \\ \hline 1 & 2 & 3 & 4 \\ \hline \% & \% & \% & \% \\ \hline \end{array}$
Integumentar	y system/appandage]				
ubcutis	abscess	<11> 0 1 0 0 ( 0) ( 9) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<d><d><d></d>000(0)(0)(0)</d></d>
	epidermal cyst	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 11) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
Respiratory :	system]				
asal cavit	mineralization	<11> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 9> 1 0 0 0 ( 11) ( 0) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre> &lt; 4&gt; 0 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>
	inflammation	0 1 0 0 (0)(9)(0)(0)	0 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	goblet cell hyperplasia	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (11) (0) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	eosinophilic change:olfactory epitheliu	m 8 0 0 0 (73)(0)(0)(0)	5 0 0 0 (56)(0)(0)(0)	4 0 0 0 (44)(0)(0)(0)	1 0 0 0 (25)(0)(0)(0)
	eosinophilic change:respiratory epithel	ium 2 0 0 0 (18)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)

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: 1

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STUDY NO.	:	0267
ANIMAL	:	RAT F344/DuCrj
REPORT TYPE	:	Λ1
SEX	:	MALE

## HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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PAGE: 2

0rgan	Findings	Group Name Co No. of Animals on Study 11 Grade <u>1 2</u> (%) (%)	ntrol $ \frac{3  4}{(\%)  (\%)}  \frac{1}{(\%)} $	750 ppm 9 <u>2 3 4</u> (%) (%) (%)	$\begin{array}{c} 1500 \text{ ppm} \\ 9 \\ \hline (\%) & (\%) & (\%) \\ \hline (\%) & (\%) & (\%) \\ \hline \end{array}$	3000 ppm 4 <u>1 2 3 4</u> (%) (%) (%) (%)
(Respiratory s	system]					
nasal cauit	inflammation:foreign body	<11 1 1 ( 9) ( 9) (	0 0 5	< 9> 1 0 0 ( 11) ( 0) ( 0)	< 9> 4 0 0 0 (44) (0) (0) (0)	<pre> &lt; 4&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>
	respiratory metaplasia:olfactory epit	nəlium 1 0 (9)(0)(	0 0 2 0) ( 0) ( 22)	0 0 0 ( 0) ( 0) ( 0)	1 0 0 0 (11)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	respiratory metaplasia:gland	2 0 (18)(0)(	0 0 3 0) (0) (33)	0 0 0 ( 0) ( 0) ( 0)	1 0 0 0 (11) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	squamous cell metaplasia:respiratory o	epithelium 20 (18)(0)(	0 0 1 0) ( 0) ( 11)	0 0 0 ( 0) ( 0) ( 0)	1 0 0 0 (11)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
lung	congestion	<111 1 0 ( 9) ( 0) (	0 0 7		< 9> 1 0 0 0 ( 11) ( 0) ( 0) ( 0)	<pre></pre>
	edema	1 0 (9)(0)(	0 0 1 (11)	0 0 0 ( 0) ( 0) ( 0)	1 0 0 0 (11) (0) (0) (0)	0 0 0 0 (0)(0)(0)(0)
[Hematopoietic	c system]					
bone marrow	consestion	<11 0 0 ( 0) ( 0) (	0 0 1		< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>

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

~gan	Findings		Control 11 <u>3 4</u> (%) (%)	750 ppm 9 <u>1 2 3 4</u> (%) (%) (%) (%)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	3000 ppm 4 <u>1 2 3 4</u> (%) (%) (%) (%)
ematopoieti	c system]					
ne marrow	hemorrhage	3 0	(11) 0 0 ( 0) ( 0)	<pre> &lt; 9&gt;     1 0 0 0     (11) (0) (0) (0) </pre>	<pre></pre>	<pre></pre>
	granulation	1 0 (9)(0)	0 0 ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	decreased hematopoiesis	0 0 ( 0) ( 0)	0 0	1 0 0 0 (11)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	erythropoiesis:increased	4 0 (36) (0)	0 0	1 0 0 0 (11)(0)(0)(0)	1 0 0 0 (11)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
.een	atrophy	2 0	(11) 0 0 ( 0) ( 0)	<pre> &lt; 8&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>	<pre></pre>	<pre> &lt; 4&gt;     1 0 0 0     ( 25) ( 0) ( 0) ( 0)</pre>
	deposit of hemosiderin	2 2 (18) (18)	0 0	8 0 0 0 ** (100) ( 0) ( 0) ( 0)	4 1 0 0 (44)(11)(0)(0)	4 0 0 0 (100) ( 0) ( 0) ( 0)
·	fibrosis	1 0 (9)(0)	0 0 ( 0) ( 0)	1 0 0 0 (13) (0) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	extramedullary hematopoiesis	4 1 (36) (9)	0 0 ( 0) ( 0)	0 1 0 0 ( 0) ( 13) ( 0) ( 0)	0 1 0 0 ( 0) ( 11) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)

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

b : Number of animals with lesion b

(c) c:b/a\*100

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

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCri

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0rgan	Findines	Group Name Control No. of Animals on Study 11 Grade <u>1 2 3 4</u> (%) (%) (%) (%)	$\begin{array}{c} 750 \text{ ppm} \\ 9 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{c} 3000 \text{ ppm} \\ 4 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$
[Circulator	у system]				
heart	thrombus	$\begin{array}{c} <11>\\ 1 & 0 & 0 \\ (9) & (0) & (0) & (0) \end{array}$	< 9> 3 0 0 0 ( 33) ( 0) ( 0) ( 0)	<pre></pre>	<pre> &lt; 4&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>
	mineralization	0 1 0 0 ( 0) ( 9) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (11)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	myocardial fibrosis	3 2 0 0 (27) (18) (0) (0)	6 0 0 0 (67)(0)(0)(0)	5 0 0 0 (56)(0)(0)(0)	2 1 0 0 (50)(25)(0)(0)
[Digestive	system]				
tooth	inflammation	$\begin{array}{c} <11>\\ 1 & 0 & 0 \\ (9) & (0) & (0) & (0) \end{array}$	<pre> &lt; 9&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>	<pre> &lt; 9&gt;     1 0 0 0     ( 11) ( 0) ( 0) ( 0)</pre>	<pre></pre>
stomach	mineralization	$\begin{array}{c} <11>\\ 0 & 0 & 1 & 0\\ ( & 0) & ( & 0) & ( & 9) & ( & 0) \end{array}$	< 9> 1 0 0 0 (11) (0) (0) (0)	< 9> 2 0 0 0 ( 22) ( 0) ( 0) ( 0)	< 4> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	ulcer:forestomach	0 0 0 1 ( 0) ( 0) ( 0) ( 9)	0 0 0 2 ( 0) ( 0) ( 0) ( 22)	0 1 0 0 ( 0) ( 11) ( 0) ( 0)	0 1 0 0 ( 0) ( 25) ( 0) ( 0)
Grade < a > b (c) Significant	1:Slight 2:Moderate a:Number of animals examined at b:Number of animals with lesion c:b/a * 100 t difference; *:P ≤ 0.05 **				

### STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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PAGE: 4

(HPT150)

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#### STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

# HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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)rgan	Findings	Group Name Control No. of Animals on Study 11 Grade <u>1 2 3 4</u> (%) (%) (%) (%)	$ \begin{array}{c} 750 \text{ ppm} \\ 9 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $	$ \begin{array}{c} 1500 \text{ ppm} \\ 9 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$\begin{array}{c} 3000 \text{ ppm} \\ 4 \\ \hline (\%) (\%) (\%) (\%) (\%) \\ (\%) \end{array}$
Digestive sy	stem]				
stomach	hyperplasia:forestomach	$\begin{pmatrix} \langle 11 \rangle \\ 0 & 1 & 0 & 0 \\ ( & 0) & ( & 3) & ( & 0) & ( & 0) \\ \end{pmatrix}$	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 9> 1 1 0 0 (11) (11) (0) (0)	<pre> &lt; 4&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>
	erosion:glandular stomach	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (11) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	ulcer:glandular stomach	0 1 0 0 ( 0) ( 9) ( 0) ( 0)	1 0 1 0 (11) (0) (11) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
arge intes	arteritis	$\begin{array}{c} \langle 11 \rangle \\ 0 & 0 & 0 \\ ( & 0) & ( & 0) & ( & 0) \\ \end{array}$	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>
iver	necrosis:central	<11> 1 2 0 0 ( 9) (18) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre> &lt; 4&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0</pre>
	fatty change	2 0 0 0 (18) (0) (0) (0)	0 0 2 0 ( 0) ( 0) ( 22) ( 0)	1 0 0 0 (11) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0
	granulation	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 11) ( 0) ( 0)	1 0 0 0 (11)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0

b: Number of animals with lesion c: b / a \* 100 b

( c )

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

(HPT150)

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STUDY NO.	:	0267
ANIMAL	:	RAT F344/DuCrj
REPORT TYPE	:	Å1
SEX	:	MALE

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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Organ	Findings	Group Name No. of Animals on Study Grade <u>1</u> (%)	Control 11 2 3 4 (%) (%) (%)	$\begin{array}{c} 750 \text{ ppm} \\ 9 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$	1500 ppm 9 <u>1 2 3 4</u> (%) (%) (%) (%)	3000 ppm 4 <u>1 2 3 4</u> (%) (%) (%) (%)
(Digestive s	ystem]					
Liver	basophilic cell focus	1 ( 9)	<11> 0 0 0 ( 0) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>
	spongiosis hepatis	1 ( 9)	0 0 0 ( 0) ( 0) ( 0)	1 0 0 0 (11) ( 0) ( 0) ( 0)	1 0 0 0 (11) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	bile duct hyperplasia	9 ( 82)	1 0 0 (9)(0)(0)	7 1 0 0 (78) (11) (0) (0)	7 1 0 0 (78) (11) (0) (0)	3 0 0 0 (75)(0)(0)(0)
pancreas	atrophy	1 ( 9)	<11> 0 0 0 ( 0) ( 0) ( 0)	< 9> 1 0 0 0 (11) (0) (0) (0)	<pre></pre>	$\langle 4 \rangle$ 0 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
[Urinary sys	tem]					
kidney	deposit of hemosiderin	1 ( 9)	<11> 0 0 0 ( 0) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>	<pre></pre>
	eosinophilic body	2 (18)	1 0 0 (9)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 1 0 0 ( 0) (25) ( 0) ( 0)
Grade < a > b	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				

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

(HPT150)

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### STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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PAGE: 7

Organ	Findings	Group Name Control No. of Animals on Study 11 Grade <u>1 2 3 4</u> (%) (%) (%) (%)	$\begin{array}{c} 750 \text{ ppm} \\ 9 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{c} 3000 \text{ ppm} \\ 4 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$
(Urinary syst	rem]				
kidney	chronic nephropathy	<11> 0 3 5 1 ( 0) ( 27) ( 45) ( 9)	< 9> 0 3 5 1 ( 0) ( 33) ( 56) ( 11)	< 9> 0 8 1 0 * ( 0) ( 89) ( 11) ( 0)	<pre></pre>
	papillary necrosis	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (11)(0)(0)(0)	3 0 0 0* (75)(0)(0)(0)
	mineralization:pelvis	1 0 0 0 (9)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	mineralization:cortex	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 0 0 0 (22)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
rin bladd	ulcer	$\begin{pmatrix} <11> \\ 0 & 1 & 0 & 0 \\ ( & 0) & ( & 9) & ( & 0) & ( & 0) \\ \end{pmatrix}$	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>
	mineralization	1 0 0 0 (9)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
(Endocrine sy	rstem]				
pituitary	hemorrhage	<11> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre> &lt; 4&gt; 0 0 1 0 ( 0) ( 0) ( 25) ( 0)</pre>

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

)rgan	Findings	Group Name Control No. of Animals on Study 11 Grade <u>1 2 3 4</u> (%) (%) (%) (%	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{c} 3000 \text{ ppm} \\ 4 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$
Endocrine s	vstem]			·····	
ituitary	necrosis:focal	<11> 1 0 0 0 ( 9) ( 0) ( 0) ( 0	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 4> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	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 (25)(0)(0)(0)
	hyperplasia	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	1 0 0 0 (11) (0) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
חערםid	C-cell hyperplasia	$\begin{array}{c} <11>\\ 1 & 0 & 0 & 0\\ (9) & (0) & (0) & (0) \end{array}$	< 9> 1 0 0 0 ( 11) ( 0) ( 0) ( 0)	< 9> 1 0 0 0 ( 11) ( 0) ( 0) ( 0)	< 4> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	focal follicular cell hyperplasia	0 0 0 0 ( 0) ( 0) ( 0) ( 0	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (11) (0) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
drenal	necrosis:focal	$\begin{array}{c} <11>\\ 1 & 0 & 0 \\ (9) & (0) & (0) \\ \end{array}$		< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre> &lt; 4&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>
	hyperplasia:medulla	1 0 0 0 (9)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 (0)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)

Grade 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

(HPT150)

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

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Drgan	Findings	Group Name No. of Animals on Study Grade <u>1</u> (%)	Control 11 <u>2 3 4</u> (%) (%) (%)	$   \begin{array}{c}     750 \text{ ppm} \\     9 \\     \hline     \frac{1  2  3  4}{(\%)  (\%)  (\%)}   \end{array} $	$\begin{array}{c} 1500 \text{ ppm} \\ 9 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
Endocrine s	vstem]					
adrena L	focal fatty change:cortex	0 ( 0)	<11> 0 0 0 ( 0) ( 0) ( 0)	< 9> 0 1 0 0 ( 0) ( 11) ( 0) ( 0)	<pre> &lt; 9&gt;     1 0 0 0     ( 11) ( 0) ( 0) ( 0)</pre>	< 4> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	cortical vacuolation:diffuse	0 ( 0)	0 0 0 ( 0) ( 0) ( 0)	1 0 0 0 (11)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
Reproductiv	e system]					
estis	atrophy	4 ( 36)	<11> 0 0 0 ( 0) ( 0) ( 0)	< 9> 1 0 0 0 ( 11) ( 0) ( 0) ( 0)	< 9> 1 0 0 0 (11) (0) (0) (0)	<pre> &lt; 4&gt;     1 0 0 0     ( 25) ( 0) ( 0) ( 0)</pre>
	mineralization	2 ( 18)	0 0 0 ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (11)(0)(0)(0)	1 0 0 0 (25)(0)(0)(0)
rostate	hyperplasia	0 ( 0)	<11> 0 0 0 ( 0) ( 0) ( 0)	< 9> 1 0 0 0 (11) (0) (0) (0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre> &lt; 4&gt; 0 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>
ammary gl	galactocele	2 ( 18)	<11> 0 0 0 ( 0) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre> &lt; 9&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>	<ul> <li>&lt; 4&gt;</li> <li>0</li> <li>0</li></ul>

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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<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)

STUDY NO. : 0267

REPORT TYPE : A1

ANIMAL : RAT F344/DuCrj

SEX	: MALE					PAGE :
Organ	Findings	Group Name Contro No. of Animals on Study 11 Grade <u>1 2 3</u> (%) (%) (%)	4	$\begin{array}{c} 750 \text{ ppm} \\ 9^{\cdot} \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	3000 ppm 4 <u>1 2 3 4</u> (%) (%) (%) (%)
[Special se	ense organs/appandage]					
өуе	cataract	$\begin{array}{c} <11>\\ 0 & 0 & 0\\ ( & 0) & ( & 0) & ( & 0) \end{array}$	0 ( 0)	<pre> &lt; 9&gt;     1 0 0 0     (11) ( 0) ( 0) ( 0)</pre>	<pre> &lt; 9&gt;     1 0 0 0     ( 11) ( 0) ( 0) ( 0) </pre>	<pre> &lt; 4&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>
	retinal atrophy	0 0 0 ( 0) ( 0) ( 0)		0 0 1 0 ( 0) ( 0) ( 11) ( 0)	1 0 0 0 (11)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	keratitis	1 1 0 (9)(9)(0)	0 ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 11) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	degeneration:cornea	2 0 0 (18) (0) (0)	0 ( 0)	1 0 0 0 (11)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (25)(0)(0)(0)

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

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

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)

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### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

GE: 10

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## APPENDIX L 3

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

RAT : MALE: SACRIFICED ANIMALS

(2-YEAR STUDY)

Organ	Group Nar No. of Ar Grade	ne Control nimals on Study 39 (%) (%) (%) (%)	$ \begin{array}{c} 750 \text{ ppm} \\ 41 \\ \underline{1 2 3 4} \\ (\%) (\%) (\%) (\%) (\%) \end{array} $	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
Integumentary	y system/appandage]				
subcutis	epidermal cyst	<39> 0 2 0 0 ( 0) ( 5) ( 0) ( 0)	<41> 0 1 0 0 ( 0) ( 2) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<46> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
Respiratory :	system]				
nasal cavit	mineralization	<39> 1 0 0 0 (3) (0) (0) (0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<46> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	inflammation	6 0 0 0 (15) (0) (0) (0)	4 1 0 0 (10) (2) (0) (0)	2 0 0 0 (5)(0)(0)(0)	0 0 0 0 (0)(0)(0)(0)(0)
	inflammatory polyp	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 1 0 0 (0)(2)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	goblet cell hyperplasia	3 0 0 0 (8)(0)(0)(0)	3 0 0 0 (7)(0)(0)(0)	4 0 0 0 (10) (0) (0) (0)	1 0 0 0 (2)(0)(0)(0)
	eosinophilic change:olfactory epithelium	36 1 0 0 (92)(3)(0)(0)	35 2 0 0 (85)(5)(0)(0)	37 1 0 0 (90)(2)(0)(0)	42 1 0 0 (91)(2)(0)(0)
	eosinophilic change:respiratory epithelium	9 0 0 0 (23)(0)(0)(0)	1 0 0 0 * (2)(0)(0)(0)	1 0 0 0 * (2)(0)(0)(0)	8 0 0 0 (17) (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 ≤ 0.05 \*\*: P ≤ 0.01 Test of Chi Square

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

STUDY NO. : 0267

#### STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

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PAGE: 2

)rgan	No	oup Name . of Animals on Study ade <u>1 2</u> (%) (%	Control 39 <u>39</u> (%) (%)	$ \begin{array}{c} 750 \text{ ppm} \\ 41 \\ \hline (\%) (\%) (\%) (\%) (\%) \end{array} $	$ \begin{array}{c} 1500 \text{ ppm} \\ 41 \\ \underline{1 \ 2 \ 3 \ 4} \\ \underline{(\%) \ (\%) \ (\%) \ (\%)} \end{array} $	$\begin{array}{c} 3000 \text{ ppm} \\ 46 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$
Respiratory	system]					
nasal cavit	inflammation:foreign body	8 0		$\langle 41 \rangle$ 15 2 0 0 (37) (5) (0) (0)	<41> 9 0 0 0 (22) (0) (0) (0)	<46> 10 1 0 0 (22) (2) (0) (0)
	respiratory metaplasia:olfactory epithel			5 0 0 0 (12) (0) (0) (0)	4 0 0 0 (10) ( 0) ( 0) ( 0)	2 0 0 0 ( 4) ( 0) ( 0) ( 0)
	respiratory metaplasia:gland	21 0 (54) (0		10 0 0 0 * (24) (0) (0) (0)	9 0 0 0 ** (22) ( 0) ( 0) ( 0)	25 0 0 0 (54)(0)(0)(0)
	squamous cell metaplasia:respiratory epi		0 0 ) ( 0) ( 0)	2 0 0 0 (5)(0)(0)(0)	3 1 0 0 (7)(2)(0)(0)	1 0 0 0 ( 2) ( 0) ( 0) ( 0)
	hyperplasia:respiratory epithelium	0 0 ( 0) ( 0		0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 1 0 ( 0) ( 0) ( 2) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
nasopharynx	mineralization	0 0	<39> 0 0 ) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<46> 2 0 0 0 ( 4) ( 0) ( 0) ( 0)
	inflammation	0 0 ( 0) ( 0		0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)(0)
lung	hemorrhage	0 0	<39> 0 0 ) ( 0) ( 0)	<11> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<46> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)

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

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

<sup>&</sup>lt; a > a : Number of animals examined at the site

b b: Number of animals with lesion

<sup>(</sup>c) c:b/a\*100

STUDY NO.	:	0267
ANIMAL	:	RAT F344/DuCrj
REPORT TYPE	:	A1
SEX	:	MALE

# HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

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PAGE: 3

0rgan	Findings	Group Name Control No. of Animals on Study 39 Grade <u>1 2 3</u> (%) (%) (%)	$ \frac{4}{(\%)} \qquad \frac{1 \ 2 \ 3 \ 4}{(\%) \ (\%) \ (\%) \ (\%) \ (\%)} $	$\begin{array}{c} 1500 \text{ ppm} \\ 41 \\ \hline (\%) & (\%) & (\%) & (\%) \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$	3000 ppm 46 <u>1 2 3 4</u> (%) (%) (%) (%)
[Respiratory	system]				
lung	inflammation	<39> 1 0 0 ( 3) ( 0) ( 0) (	0     2     0     0       0)     (5)     (0)     (0)     (0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<46> 3 0 0 0 ( 7) ( 0) ( 0) ( 0)
	osseous metaplasia	2 0 0 (5)(0)(0)(	0 0 0 0 0 0 0) ( 0) ( 0) ( 0) ( 0)	0 0 0 0 (0)(0)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	accumulation of foamy cells	0 0 0 ( 0) ( 0) ( 0) (	0 1 0 0 0 0) ( 2) ( 0) ( 0) ( 0)	4 0 0 0 (10) (0) (0) (0)	3 0 0 0 (7)(0)(0)(0)
	bronchiolar—alveolar cell hyperplasia	a 3 1 0 ( 8) ( 3) ( 0) (	0 1 0 0 0 0) (2) (0) (0) (0)	4 0 0 0 (10) (0) (0) (0)	1 1 0 0 (2)(2)(0)(0)
[Hematopoieti	c system]				
xone marrow	congestion	<39> 2 0 0 ( 5) ( 0) ( 0) (	<pre> &lt;41&gt; 0 1 0 0 0 0) ( 2) ( 0) ( 0) ( 0)</pre>	<pre> &lt;41&gt; 3 0 0 0 ( 7) ( 0) ( 0) ( 0)</pre>	<46> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)
	hemorrhage	3 0 0 (8)(0)(0)(	0 5 0 0 0 0) (12) (0) (0) (0)	0 0 0 0 (0)(0)(0)(0)	0 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	granulation	1 0 0 (3)(0)(0)(	0 0 0 0 0 0) ( 0) ( 0) ( 0) ( 0)	2 0 0 0 (5)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)

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

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

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PAGE: 4

0rgan	Findings	Group Name         Control           No. of Animals on Study         39           Grade         1         2         3         4	$ \begin{array}{c} 750 \text{ ppm} \\ 41 \\ \hline (\%) (\%) (\%) (\%) (\%) \end{array} $	$ \begin{array}{c} 1500 \text{ ppm} \\ 41 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
[Hematopoieti	c system]				
bone marrow	decreased hematopoiesis	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0		<41> 0 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<46> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)
	erythropoiesis:increased	6 0 0 0 (15)(0)(0)(0)	3 0 0 0 (7)(0)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)
lymph node	lymphadenitis	<39> 1 0 0 0 (3)(0)(0)(0)		<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<46> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
spleen	congestion	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0		<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<46> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)
	hemorrhage	0 0 0 0 ( 0) ( 0) ( 0) ( 0		0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)
	deposit of hemosiderin	29 0 0 0 (74)(0)(0)(0)		36 0 0 0 (88)(0)(0)(0)	26 0 0 0 (57)(0)(0)(0)
	granulation	0 0 0 0 ( 0) ( 0) ( 0) ( 0		1 0 0 0 (2)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)

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

b b : Number of animals with lesion

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

(HPT150)

		·			PAGE
rgan	Findings	Group Name         Control           No. of Animals on Study         39           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%)	$\begin{array}{c} 750 \text{ ppm} \\ 41 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%)  (\%) \end{array}$	$ \begin{array}{c} 1500 \text{ ppm} \\ 41 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%)  (\%) \end{array} $	3000 ppm 46 <u>1 2 3 4</u> (%) (%) (%) (%)
iematopoieti	c system]	·····			
oleen	fibrosis	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<41> 4 0 0 0 (10) (0) (0) (0)	<46> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)
	extramedullary hematopoiesis	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	9 1 0 0 (22)(2)(0)(0)	7 0 0 0 (17)(0)(0)(0)	11 0 0 0 (24) ( 0) ( 0) ( 0)
	fatty metamorphosis	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
Circulatory	system]				
əar-t	myocardial fibrosis	<pre> &lt;39&gt;     27 0 0 0     ( 69) ( 0) ( 0) ( 0)</pre>	<pre>&lt;41&gt; 26 2 0 0 (63) (5) (0) (0)</pre>	<41> 22 0 0 0 (54) (0) (0) (0)	<46> 26 0 0 0 (57) (0) (0) (0)
rtery/aort	arteritis	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<46> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
Digestive sy	stem]				
ooth	inflammation	<39> 3 0 0 0 ( 8) ( 0) ( 0) ( 0)	<41> 5 0 0 0 ( 12) ( 0) ( 0) ( 0)	<41> 5 0 0 0 ( 12) ( 0) ( 0) ( 0)	<46> 9 0 0 0 (20) ( 0) ( 0) ( 0)

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

STUDY NO.	:	0267
ANIMAL	:	RAT F344/DuCrj
REPORT TYPE	:	A1
SEX	:	MALE

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

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SEX :	MALE			····	PAGE : 6
0rgan	Findings	Group Name Control No. of Animals on Study 39 Grade <u>1 2 3 4</u> (%) (%) (%) (%)	$ \begin{array}{c} 750 \text{ ppm} \\ 41 \\ \hline (\%) (\%) (\%) (\%) (\%) \end{array} $	$ \begin{array}{c} 1500 \text{ ppm} \\ 41 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
(Digestive sy	rstem]				
stomach	ulcer:forestomach	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)		<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<46> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	erosion:glandular stomach	$\begin{pmatrix} 1 & 0 & 0 & 0 \\ ( & 3) & ( & 0) & ( & 0) \\ \end{pmatrix}$		0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 0 0 0 ( 4) ( 0) ( 0) ( 0)
	hemorrhage:glandular stomach	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 (2)(0)(0)(0)
large intes	mineralization	<39> 3 1 0 0 ( 8) ( 3) ( 0) ( 0)	<41> 2 0 0 0 ( 5) ( 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<46> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	Lymphangiectasia	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 (2)(0)(0)(0))
liver	herniation	<39> 2 0 0 0 (5) (0) (0) (0)		<41> 2 0 0 0 ( 5) ( 0) ( 0) ( 0)	<46> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	hemorr hage	0 0 0 0 ( 0) ( 0) ( 0) ( 0)		1 0 0 0 (2)(0)(0)(0)	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 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

STUDY NO.	:	0267
ANIMAL	:	RAT F344/DuCrj
REPORT TYPE	:	A1
SEX	:	MALE

# HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

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PAGE: 7

Organ	Findings	Group Name Control No. of Animals on Study 39 Grade <u>1 2 3 4</u> (%) (%) (%) (%)	$\begin{array}{c} 750 \text{ ppm} \\ 41 \\ \hline \\ 6 \\ \hline \\ \hline$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	3000 ppm 46 <u>1 2 3 4</u> (%) (%) (%) (%)
Digestive	system]				
liver	peliosis-like lesion	<39> 1 0 0 0 ( 3) ( 0) ( 0) ( 0	<pre>&lt;41&gt; 6 0 0 0 (15) (0) (0) (0)</pre>	<41> 6 0 0 0 (15) (0) (0) (0)	<46> 3 0 0 0 ( 7) ( 0) ( 0) ( 0)
	necrosis:focal	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	) 1 0 0 0 (2) (0) (0) (0)	1 0 0 0 (2)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	fatty change	2 0 0 0 (5)(0)(0)(0)	2 0 0 0 (5) (0) (0) (0)	3 0 0 0 (7)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)(0)
	fatty change:peripheral	0 0 0 0 ( 0) ( 0) ( 0) ( 0	1 0 0 0 (2) (0) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	inflammatory infiltration	1 0 0 0 (3)(0)(0)(0	0 0 0 0 ) ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	sranulation	14 1 0 0 (36)(3)(0)(0	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	8 1 0 0 (20)(2)(0)(0)	3 1 0 0 ** (7)(2)(0)(0)
	clear cell focus			8 1 0 0 (20)(2)(0)(0)	3 0 0 0 ** (7)(0)(0)(0)
	acidophilic cell focus	9 0 0 0 (23)(0)(0)(0)		1 0 0 0 * (2)(0)(0)(0)	3 0 0 0 (7)(0)(0)(0)

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

b: Number of animals with lesion c: b / a \* 100 b

(c)

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

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

14-1

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0rgan	Findings	Group Name Control No. of Animals on Study 39 Grade <u>1 2 3 4</u> (%) (%) (%) (%)	$\begin{array}{c} 750 \text{ ppm} \\ 41 \\ \hline (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$	$ \begin{array}{c}     1500 \text{ ppm} \\     41 \\     \underline{1  2  3  4} \\     (\%)  (\%)  (\%)  (\%) \end{array} $	$ \begin{array}{c} 3000 \text{ ppm} \\ 46 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $
Digestive s	vstem]				
iver	basophilic cell focus	<39> 10 1 0 0 (26) (3) (0) (0)	<41> 7 0 0 0 (17) (0) (0) (0)	<41> 5 0 0 0 (12) ( 0) ( 0) ( 0)	<46> 7 0 0 0 (15) (0) (0) (0)
	vacuplated call focus	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	4 0 0 0 (10) (0) (0) (0)	4 0 0 0 (10)(0)(0)(0)	4 0 0 0 (9)(0)(0)(0)
	mixed cell focus	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	2 0 0 0 (5)(0)(0)(0)	2 0 0 0 (5)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	spongiosis hepatis	10 0 0 0 (26)(0)(0)(0)	10 0 0 0 (24) ( 0) ( 0) ( 0)	8 1 0 0 (20)(2)(0)(0)	2 0 0 0 ( 4) ( 0) ( 0) ( 0)
	bile duct hyperplasia	34 5 0 0 (87)(13)(0)(0)	32 9 0 0 (78)(22)(0)(0)	37 4 0 0 (90) (10) (0) (0)	42 2 0 0 (91)(4)(0)(0)
ancreas	atrophy	<39> 4 0 0 0 (10) (0) (0) (0)	<41> 10 2 0 0 (24) (5) (0) (0)	<41> 13 0 0 0 * ( 32) ( 0) ( 0) ( 0)	<46> 10 1 0 0 (22) (2) (0) (0)
Irinary syst	em]				
dhey	basophilic change	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<46> 1 1 0 0 ( 2) ( 2) ( 0) ( 0)

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

PAGE: 8

STUDY NO.	:	0267
ANIMAL	:	RAT F344/DuCrj
REPORT TYPE	:	A1
SEX	:	MALE

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

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SEX	: MALE				PAGE : 9
Organ	Findings	Group Name Control No. of Animals on Study 39 Grade <u>1 2 3 4</u> (%) (%) (%) (%)	$ \begin{array}{c} 750 \text{ ppm} \\ 41 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$ \begin{array}{c} 1500 \text{ ppm} \\ 41 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$ \begin{array}{c} 3000 \text{ ppm} \\ 46 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $
[Urinary sy	stem]				······································
kidney	deposit of hemosiderin	<39> 1 1 0 0 (3) (3) (0) (0)	<41> 5 0 0 0 (12) (0) (0) (0)	<41> 4 0 0 0 (10) (0) (0) (0)	<46> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)
	easinaphilic body	9 0 0 0 (23)(0)(0)(0)	10 0 0 0 (24)(0)(0)(0)	8 0 0 0 (20)(0)(0)(0)	8 0 0 0 (17)(0)(0)(0)
	chronic nephropathy	0 11 26 2 ( 0) ( 28) ( 67) ( 5)	1 16 17 7 (2)(39)(41)(17)	0 25 16 0 ** ( 0) ( 61) ( 39) ( 0)	5 36 5 0 ** (11) (78) (11) (0)
	papillary necrosis	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)	8 0 0 0 * (20) ( 0) ( 0) ( 0)	20 1 0 0 <b>**</b> (43) (2) (0) (0)
	mineralization:peluis	$\begin{pmatrix} 1 & 0 & 0 & 0 \\ (3) & (0) & (0) & (0) \end{pmatrix}$	1 0 0 0 (2)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
[Endocrine :	system]				
pituitary	angiectasis	<39> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	<41> 0 1 0 0 ( 0) ( 2) ( 0) ( 0)	$\begin{array}{c} <41>\\ 1 & 0 & 1 & 0\\ (2) & (0) & (2) & (0) \end{array}$	<46> 1 1 0 0 ( 2) ( 2) ( 0) ( 0)
	hemorrhage	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 (2) (0) (0) (0)
Grada	1 . 01. 1.				

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

a : Number of animals examined at the site b : Number of animals with lesion <a>>

b

(c) c:b/a\*100

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

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

<u> </u>					PAGE :
0rgan	Findings	Group Name     Control       No. of Animals on Study     39       Grade     1     2     3     4       (%)     (%)     (%)     (%)     (%)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$ \begin{array}{c} 1500 \text{ ppm} \\ 41 \\ \underline{1  2  3  4} \\ \underline{(\%)  (\%)  (\%)  (\%)} \end{array} $	$\begin{array}{c} 3000 \text{ ppm} \\ 46 \\ \hline 1 & 2 & 3 & 4 \\ \hline \% & (\%) & (\%) & (\%) & (\%) \end{array}$
(Endocrine sy	vstem]				
pituitary	necrosis:focal	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<46> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	cyst	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	4 0 0 0 (10)(0)(0)(0)	3 0 0 0 (7)(0)(0)(0)	2 0 0 0 (4)(0)(0)(0)
	deposit of hemosiderin	2 0 0 0 (5)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 0 0 0 (5)(0)(0)(0)	2 0 0 0 (4)(0)(0)(0)
	hyperplasia	6 8 0 0 (15) (21) (0) (0)	11 2 0 0 (27) (5) (0) (0)	5 5 1 0 (12)(12)(2)(0)	8 3 1 0 (17)(7)(2)(0)
	Rathke pouch	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)	2 0 0 0 (5)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)
thyroid	hemorrhage	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre> &lt;41&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>	<41> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<46> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)
	cyst	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)
	C-cell hyperplasia	3 0 0 0 (8)(0)(0)(0)	3 0 0 0 (7)(0)(0)(0)	8 1 0 0 (20)(2)(0)(0)	3 1 0 0 (7)(2)(0)(0)

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

a : Number of animals examined at the site b : Number of animals with lesion <a>

b

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

PAGE : 10

#### STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

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0rgan	Findings		Control 39 <u>34</u> (%) (%)	$\begin{array}{c} 750 \text{ ppm} \\ 41 \\ \hline (\%) & (\%) & (\%) & (\%) \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$	$ \begin{array}{c} 1500 \text{ ppm} \\ 41 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$ \begin{array}{c} 3000 \text{ ppm} \\ 46 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $
Endocrine s	system]					
thyroid	focal follicular cell hyperplasia	1 0	39> 0 0 ( 0) ( 0)	<41> 3 1 0 0 ( 7) ( 2) ( 0) ( 0)	<41> 2 0 0 0 ( 5) ( 0) ( 0) ( 0)	<46> 1 1 0 0 ( 2) ( 2) ( 0) ( 0)
anc islet	islet cəll hyperplasia	2 0	39> 0 0 ( 0) ( 0)	<41> 2 0 0 0 ( 5) ( 0) ( 0) ( 0)	<pre>&lt;41&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>	<46> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)
drenal.	peliosis-like lesion	< 0 0 ( 0) ( 0)	39> 0 0 ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<46> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)
	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)	0 1 0 0 ( 0) ( 2) ( 0) ( 0)
	hyperplasia:cortical cell	1 0 (3)(0)	0 0 (0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 0 0 0 (4)(0)(0)(0)
	hyperplasia:medulla	6 2 (15)(5)	0 0 ( 0) ( 0)	2 0 0 0 (5)(0)(0)(0)	2 0 0 0 (5)(0)(0)(0)	2 0 0 0 (4)(0)(0)(0)
	focal fatty change:cortex	3 0 (8)(0)	0 0 (0)(0)	6 0 0 0 (15)(0)(0)(0)	2 0 0 0 (5)(0)(0)(0)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$

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

(HPT150)

PAGE : 11

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

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PAGE: 12

0rgan	Findings	Group Name No. of Animals on Study Grade <u>1</u> (%)	Control 39 <u>2 3 4</u> (%) (%) (%)	$\begin{array}{c} 750 \text{ ppm} \\ 41 \\ \underline{1  2  3  4} \\ \hline (\%)  (\%)  (\%)  (\%) \end{array}$	$ \begin{array}{c} 1500 \text{ ppm} \\ 41 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$ \begin{array}{c} 3000 \text{ ppm} \\ 46 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $
[Reproductive	o system]					
testis	atrophy	5 (13) (	<39> 0 0 0 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 4 0 0 0 ( 10) ( 0) ( 0) ( 0)	<46> 2 0 0 0 ( 4) ( 0) ( 0) ( 0)
	mineralization	4 (10) (	0 0 0 0)(0)(0)	1 0 0 0 (2)(0)(0)(0)	2 0 0 0 (5)(0)(0)(0)	7 0 0 0 (15)(0)(0)(0)
	interstitial cell hyperplasia	0 ( 0) (	0 0 0 0)(0)(0)	2 0 0 0 (5)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
prostate	granulation	( 0) (	<39> 0 0 0 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<46> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)
	hyperplasia	8 (21)(1	5 0 0 3)(0)(0)	3 0 0 0 ** (7)(0)(0)(0)	8 2 0 0 (20)(5)(0)(0)	4 1 0 0 * (9)(2)(0)(0)
mammary gl	galactocele	0 ( 0) (	<39> 0 0 0 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<46> 2 0 0 0 ( 4) ( 0) ( 0) ( 0)
prep/cligl	inflammation	0 ( 0) ( 1	<39> 1 0 0 3) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<46> 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 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

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

Organ\_

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

(%)

(%)

(%)

2

(%)

(%)

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Group Name

Grade

No. of Animals on Study

0 3	iontrol 9			71 41	50 ppm 1			15 4	00 ppm 1	
?	3	4	1	2	3	4	1	2	- 3	Δ
	(6/)									

(%)

(%)

(%)

(%)

(%) (%) (%)

[Special sense organs/appandage]

Findings\_

• • • • • • • • • • • •				
еуе	cataract	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	<pre></pre>	<46> 2 1 0 0 ( 4) ( 2) ( 0) ( 0)
	retinal atrophy	1 3 0 0 2 3 0 (3) (8) (0) (0) (5) (7) (0)	0 1 1 1 0 ( 0) ( 2) ( 2) ( 2) ( 0)	1 2 0 0 (2)(4)(0)(0)
	keratitis	1 0 0 0 0 0 0 (3)(0)(0)(0)(0)(0)(0)(0)(0)	0 0 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 (0)(0)(0)(0)(0)
	degeneration:cornea vascularization:cornea	5       0       0       0       0       0         (13)       (0)       (0)       (0)       (0)       (0)       (0)		3 0 0 0 (7)(0)(0)(0)
Xarder gl				0 0 0 0 (0)(0)(0)(0)
nasolaor d	granulation	(395)       (415)         0       0       0       0       0         (0)       (0)       (0)       (0)       (0)       (0)	$\begin{pmatrix} 41 \\ 0 \\ 1 \\ 0 \\ 0 \end{pmatrix} = \begin{pmatrix} 41 \\ 0 \\ 0 \\ 0 \end{pmatrix} = \begin{pmatrix} 41 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$	<46> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
HASULACE Q	inflammation	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	<pre></pre>	<46> 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)

PAGE: 13

<u>4</u> (%)

3000 ppm

3

(%)

46

2

(%)

(%)

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

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| Organ                  | Findings                                                                                                                                                     | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | 39<br>2             | trol<br>3<br>(%) | 4 (%)   | <u>1</u><br>(%) | 75<br>41<br>(%)    | 50 ppm<br>3 4<br>(%) (%) | <u>1</u><br>(%) |                 | 00 ppm<br>1<br><u>3</u><br>(%) | 4 (%)     | 1(%)        | 300<br>46<br><u>2</u><br>(%) | 00 ppm<br>3<br><u>3</u><br>(%) | 4 (%) |
|------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|---------------------|------------------|---------|-----------------|--------------------|--------------------------|-----------------|-----------------|--------------------------------|-----------|-------------|------------------------------|--------------------------------|-------|
| (Musculosk             | eletal system]                                                                                                                                               |                                                                |                     |                  |         |                 |                    |                          |                 |                 |                                |           |             |                              |                                |       |
| Dine                   | asteasclerasis                                                                                                                                               | 0<br>( 0)                                                      | <39><br>0<br>( 0) ( | 0<br>0) (        | 0<br>0) | 1<br>(2)        | <41<br>0<br>( 0) ( | 0 0                      | 1<br>( 2)       | <4<br>0<br>( 0) | 1><br>0<br>( 0) (              | 0<br>( 0) | 0<br>( 0) ( | <46<br>0<br>0) (             | 3><br>0<br>( 0) (              | 0     |
| rade<br>a ≻<br>b<br>c) | 1: Slight 2: Moderate<br>a: Number of animals examined at the<br>b: Number of animals with lesion<br>c: b / a * 100<br>t difference; $*: P \leq 0.05  **: P$ |                                                                |                     |                  |         |                 |                    |                          |                 |                 |                                |           |             |                              |                                |       |

BAIS3

# APPENDIX L 4

# HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : ALL ANIMALS

(2-YEAR STUDY)

| STUDY NO.   | : | 0267           |
|-------------|---|----------------|
| ANIMAL      | : | RAT F344/DuCrj |
| REPORT TYPE | : | A1             |
| SEX         | : | FEMALE         |

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

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| •••            |                           |                                                                                             |                                                       |                                                                                                                   | PAGE : 1                                            |
|----------------|---------------------------|---------------------------------------------------------------------------------------------|-------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------|
| 0rgan          | Findings                  | Group Name Control<br>No. of Animals on Study 50<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{c} 1500 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | 3000 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| [Integumentar  | ry system/appandage]      |                                                                                             |                                                       |                                                                                                                   |                                                     |
| skin/app       | ulcer                     | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                      | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <50><br>5 0 0 0<br>(10) (0) (0) (0)                                                                               | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)              |
|                | squamous cell hyperplasia | 0 0 0 0<br>(0)(0)(0)(0)                                                                     | 0 0 0 0<br>(0)(0)(0)(0)(0)                            | 2 0 0 0<br>(4)(0)(0)(0)                                                                                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      |
| [Respiratory : | system]                   |                                                                                             |                                                       |                                                                                                                   |                                                     |
| nasal cavit    | ulcer                     | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                      | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                            | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |
|                | hemorrhage                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                              | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 1 0 0 0<br>(2)(0)(0)(0)                                                                                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      |
|                | mineralization            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 1 0 0 0<br>(2)(0)(0)(0)                                                                                           | 1 0 0 0<br>(2)(0)(0)(0)                             |
|                | inflammation              | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$                                       | 1 0 0 0<br>(2)(0)(0)(0)(0)                            | 3 0 0 0<br>(6)(0)(0)(0)                                                                                           | 2 0 0 0<br>(4)(0)(0)(0)                             |
|                | hyperplasia:gland         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                              | 1 0 0 0<br>(2)(0)(0)(0)                               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                    | 1 0 0 0<br>(2)(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

| 0rgan        |                                             | Name         Control           of Animals on Study         50           a         1         2         3         4           (%)         (%)         (%)         (%)         (%) | 750 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%)         | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{c} 3000 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ |
|--------------|---------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------|-------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|
| [Respiratory | system]                                     |                                                                                                                                                                                 |                                                            |                                                       |                                                                                                                 |
| nasal cavit  | goblet cell hyperplasia                     | <50><br>8 0 0 0<br>( 16) ( 0) ( 0) ( 0)                                                                                                                                         | <50><br>7 0 0 0<br>(14) (0) (0) (0)                        | <50><br>3 1 0 0<br>( 6) ( 2) ( 0) ( 0)                | <50><br>4 1 0 0<br>( 8) ( 2) ( 0) ( 0)                                                                          |
|              | eosinophilic change:olfactory epithelium    | 44 2 0 0<br>(88) (4) (0) (0)                                                                                                                                                    | 45 1 0 0<br>(90)(2)(0)(0)                                  | 45 4 0 0<br>(90)(8)(0)(0)                             | 29 17 0 0 **<br>(58) (34) (0) (0)                                                                               |
|              | eosinophilic change:respiratory epithelium  | 3 0 0 0<br>(6)(0)(0)(0)                                                                                                                                                         | 14 0 0 0 ***<br>(28) (0) (0) (0)                           | 13 0 0 0 *<br>(26)(0)(0)(0)                           | 8 0 0 0<br>(16)(0)(0)(0)                                                                                        |
|              | inflammation:foreign body                   | 3 0 0 0<br>(6)(0)(0)(0)                                                                                                                                                         | 3 0 0 0<br>(6)(0)(0)(0)                                    | 4 0 0 0<br>(8)(0)(0)(0)                               | 4 0 0 0<br>(8)(0)(0)(0)                                                                                         |
|              | respiratory metaplasia:gland                | 12 0 0 0<br>(24) (0) (0) (0)                                                                                                                                                    | 11 0 0 0<br>(22) (0) (0) (0)                               | 16 0 0 0<br>(32)(0)(0)(0)                             | 15 0 0 0<br>(30)(0)(0)(0)                                                                                       |
|              | squamous cell metaplasia:respiratory epithe | əlium 30000<br>(6)(0)(0)(0)                                                                                                                                                     | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                             | 3 0 0 0<br>(6)(0)(0)(0)                               | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                                                                                  |
| larynx       | ulcer                                       | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                          | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                                          |
| lung         | congestion                                  | <50><br>4 0 0 0<br>( 8) ( 0) ( 0) ( 0)                                                                                                                                          | <pre> &lt;50&gt;     2 0 0 0     ( 4) ( 0) ( 0) ( 0)</pre> | <50><br>3 0 0 0<br>( 6) ( 0) ( 0) ( 0)                | <50><br>3 0 0 0<br>( 6) ( 0) ( 0) ( 0)                                                                          |
| Grade        | 1:Slight 2:Moderate 3:Mar                   | rked 4 : Severe                                                                                                                                                                 |                                                            |                                                       |                                                                                                                 |

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

# STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

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

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(HPT150)

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

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|                |                                       | Group Name<br>No. of Animals on Study | Contr<br>50         |               |                | 50                 |                   |         | 1         |           | 1500 i<br>50 |            | 4        |   |             | 300<br>50        |                 |           |
|----------------|---------------------------------------|---------------------------------------|---------------------|---------------|----------------|--------------------|-------------------|---------|-----------|-----------|--------------|------------|----------|---|-------------|------------------|-----------------|-----------|
| )rgan          | Findings                              | Grade <u>1</u><br>(%)                 | 2<br>(%) (%         | 3 4<br>%) (%  |                | 2<br>(%)           | 3 (%)             | 4 (%)   | (%)       | (%)       |              | 3<br>%)    | 4<br>(%) | ( | i<br>%)     | (%)              | 3<br>(%)        | 4(%)      |
| Respiratory s  | ystem]                                |                                       |                     |               |                |                    | ·                 |         |           |           |              |            |          |   |             |                  |                 |           |
| lung           | hemorrhage                            | 4<br>( 8)                             | <50><br>0<br>( 0) ( | 0 (<br>0) ( ( |                | <50<br>0<br>( 0) ( | ><br>0<br>0) (    | 0<br>0) | 0<br>( 0) | 0         |              | 0<br>0) (  | 0<br>0)  |   | 0<br>0) (   | <50<br>0<br>0) ( | )><br>0<br>( 0) | 0<br>( 0) |
|                | deposit of hemosiderin                | 1<br>( 2)                             | 0 ( 0) (            | 0 (<br>0)((   |                | 0<br>( 0) (        | 0<br>0) (         | 0<br>0) | 0<br>( 0) | 0         |              | 0<br>0) _( | 0<br>0)  |   | 0<br>0) (   | 0<br>0) (        | 0<br>( 0)       | 0<br>( 0) |
|                | granulation                           | 0<br>( 0)                             | 0<br>( 0) (         | 0 (<br>0) ( ( | ) 0<br>)) (0)  | 0<br>( 0) (        | 0<br>( 0) (       | 0<br>0) | 2<br>( 4) | 0<br>( 0) | ) (          | 0<br>0) (  | 0<br>0)  | ( | 2<br>4) (   | 0<br>0)          | 0<br>( 0)       | 0<br>( 0) |
|                | accumulation of foamy cells           | 2<br>( 4)                             | 0<br>( 0) (         |               | ) 3<br>)) (6)  | 0<br>( 0) (        | 0<br>( 0) (       | 0<br>0) | 5<br>(10) | 0         |              | 0<br>0) (  | 0<br>0)  |   | .4<br>28) ( | 1<br>2)          | 0<br>( 0)       | 0<br>( 0) |
|                | bronchiolar-alveolar cell hyperplasia |                                       | 1<br>(2)(           |               | 0 0<br>0) ( 0) | 2<br>( 4) (        | 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) |
| [Hematopoietic | : system]                             |                                       |                     |               |                |                    |                   |         |           |           |              |            |          |   |             |                  |                 |           |
| oone marrow    | congestion                            | ( 2)                                  | <50><br>0<br>( 0) ( |               | 0 1<br>0) (2)  | <5(<br>0<br>( 0) ( | )><br>0<br>( 0) ( | 0<br>0) | 0<br>( 0) | 0         |              | 0<br>0) (  | 0<br>0)  | ( | 3<br>6) (   | <50<br>0<br>0)   | 0><br>0<br>( 0) | 0<br>( 0) |
|                | hemorrhage                            | 3<br>( 6)                             | 0<br>( 0) (         |               | 0 0<br>0) ( 0) | 0                  | 0<br>( 0) (       | 0<br>0) | 0<br>( 0) | 0         |              | 0<br>0) (  | 0<br>0)  | ( | 3<br>6) (   | 0<br>0)          | 0<br>( 0)       | 0         |

(c) c:b/a\*100

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

|                    | indings                  | Grade <u>1 2 3</u><br>(%) (%) (%) | $\frac{4}{(\%)} \qquad \frac{1}{(\%)} \qquad \frac{2}{(\%)} \qquad \frac{3}{(\%)} \qquad \frac{3}$ | $\frac{4}{(\%)}$ $\frac{1}{(\%)}$ (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
|--------------------|--------------------------|-----------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------|-------------------------------------------------------|-------------------------------------------------------|
| (Hematopoietic sys | rstem]                   |                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                       |                                                       |                                                       |
| bone marrow<br>91  | ranulation               | <50><br>2 0 0<br>( 4) ( 0) ( 0)   | <pre></pre>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 0 0<br>) ( 0) ( 0) (                  | <50><br>0 0 0<br>0) ( 0) ( 0) (                       | <50><br>4 0 0 0<br>8) ( 0) ( 0) ( 0)                  |
| d                  | decreased hematopoiesis  | 0 0 0<br>( 0) ( 0) ( 0)           | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 0 0<br>) ( 0) ( 0) (                  | 0 0 0<br>0)(0)(0)(                                    | 2 0 0 0<br>4) ( 0) ( 0) ( 0)                          |
| 8                  | erythropoiesis:increased | 3 0 0<br>(6)(0)(0)                | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 0 2<br>)(0)(4)(                       | 0 0 0<br>0)(0)(0)(()                                  | 0 0 0 0<br>0) ( 0) ( 0) ( 0)                          |
| lymph node<br>e    | ectopic tissue           | <50><br>0 0 0<br>( 0) ( 0) ( 0)   | <50><br>0 0 0 0<br>( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 0 0<br>) ( 0) ( 0) (                  | <50><br>0 0 0<br>0) ( 0) ( 0) (                       | <50><br>1 0 0 0<br>2) ( 0) ( 0) ( 0)                  |
| spleen<br>C        | congestion               | <50><br>0 0 0<br>( 0) ( 0) ( 0)   | <50><br>0 0 0 0<br>( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 0 0<br>) ( 0) ( 0) (                  | <50><br>0 0 0<br>0) ( 0) ( 0) (                       | <50><br>1 0 0 0<br>2) ( 0) ( 0) ( 0)                  |
| h                  | nemorr hage              | 1 0 0<br>(2)(0)(0)                | 0 0 0 0<br>( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 0 0<br>0 ( 0) ( 0) (                  | 0 0 0<br>0)(0)(0)(                                    | 0 0 0 0<br>0) ( 0) ( 0) ( 0)                          |
| d                  | leposit of hemosiderin   | 34 1 0<br>(68) (2) (0)            | 0 33 3 0<br>( 0) ( 66) ( 6) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0 27<br>)(0)(54)(                     |                                                       | 18 4 0 0 **<br>36) ( 8) ( 0) ( 0)                     |

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

b : Number of animals with lesion b

c:b/a\*100 (c)

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

(HPT150)

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

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

| · AI<br>: FEMALE             |                                                                                                                                                                     |                                                                                                                         |                                                                                                                          | PAGE: 20                                                                                  |
|------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|
| Findings                     | Group Name Control<br>No. of Animals on Study 50<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%)                                                                         | $ \begin{array}{c} 750 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ \hline (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $ \begin{array}{c} 1500 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | $\begin{array}{c} 3000 \text{ ppm} \\ 50 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ |
| tic system]                  |                                                                                                                                                                     |                                                                                                                         |                                                                                                                          |                                                                                           |
| fibrosis                     | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                              | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                  | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | <50><br>1 1 0 0<br>( 2) ( 2) ( 0) ( 0)                                                    |
| extramedullary hematopoiesis | 13 3 0 0<br>(26)(6)(0)(0)                                                                                                                                           | 14 3 0 0<br>(28) (6) (0) (0)                                                                                            | 14 1 0 0<br>(28) (2) (0) (0)                                                                                             | 13 1 0 0<br>(26)(2)(0)(0)                                                                 |
| v system]                    |                                                                                                                                                                     |                                                                                                                         |                                                                                                                          |                                                                                           |
| thrombus                     | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                                                                                              | <50><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                                                                                  | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                                                   | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                    |
| necrosis:focal               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                           | 0 0 3 0<br>( 0) ( 0) ( 6) ( 0)                                                            |
| mineralization               | 1 0 0 0<br>(2)(0)(0)(0)(0)                                                                                                                                          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                            |
| myocardial fibrosis          | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                                                                | 15 2 0 0<br>(30) (4) (0) (0)                                                                                            | 15 0 0 0<br>(30)(0)(0)(0)                                                                                                | 13 1 0 0<br>(26)(2)(0)(0)                                                                 |
| endocarditis                 | $\begin{pmatrix} 0 & 1 & 0 & 0 \\ ( & 0) & ( & 2) & ( & 0) & ( & 0) \end{pmatrix}$                                                                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                          | 1 0 0 0<br>(2)(0)(0)(0)                                                                                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                            |
|                              | : FEMALE<br>Findings<br>cic system]<br>fibrosis<br>extramedullary hematopoiesis<br>v system]<br>thrombus<br>necrosis:focal<br>mineralization<br>myocardial fibrosis | $\begin{array}{c ccccccccccccccccccccccccccccccccccc$                                                                   | $\begin{array}{c c c c c c c c c c c c c c c c c c c $                                                                   | $\begin{array}{c c c c c c c c c c c c c c c c c c c $                                    |

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

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

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

| 0267<br>RAT F344/DuCrj<br>A1<br>FEMALE | ALL ANIMALS (0-105W)                                                                                                                                                                                   | NEOPLASTIC LESIONS (SUMMARY)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                  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|                                        | RAT F344/DuCrj<br>A1<br>FEMALE<br>Findings<br>stem]<br>ulcer<br>inflammation<br>mineralization<br>ulcer:forestomach<br>hyperplasia:forestomach<br>erosion:glandular stomach<br>ulcer:glandular stomach | RAT       F344/DuCrj       ALL       ANIMALS $(0-105\%)^{-1}$ FEMALE       Group Name       Control       50         Findines $(3)$ $(3)$ $(3)$ $(3)$ stem]       ulcer $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ inflammation $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ mineralization $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ ulcer:forestomach $(0)$ $(0)$ $(2)$ $(0)$ $(0)$ $(0)$ ulcer:slandular stomach $(1)$ $(0)$ $(0)$ $(0)$ $(0)$ ulcer:slandular stomach $(2)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(2)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ | $\begin{array}{c} \operatorname{RAT} \operatorname{FS44/DLCrj} \\ \operatorname{AL} \\ \operatorname{AIL} \operatorname{ANIHALS} (0-105 \operatorname{W}) \\ \operatorname{AIL} \operatorname{AIL} \operatorname{ANIHALS} (0-105 \operatorname{W}) \\ \operatorname{AIL} \operatorname{AIL} \operatorname{ANIHALS} (0-105 \operatorname{W}) \\ \operatorname{AIL} $ | State 2 and 2 |

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

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

b b: Number of animals with lesion

c:b/a\*100 (c)

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

(HPT150)

BAIS3

| STUDY NO.   | : | 0267           |
|-------------|---|----------------|
| ANIMAL      | : | RAT F344/DuCrj |
| REPORT TYPE | : | A1             |
| SEX         | : | FEMALE         |

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

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PAGE : 22

Organ	Findings	Group Name No. of Animals on Study Grade <u>1</u> (%)	Control 50 <u>2 3 4</u> (%) (%) (%)	$ \begin{array}{c} 750 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{c} 3000 \text{ ppm} \\ 50 \\ \hline (\%) (\%) (\%) (\%) (\%) (\%) \end{array}$
Digestive sy	stem]					
large intes	mineralization	1	<50> 0 0 0 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
Liver	herniation	5 (10)	<50> 0 0 0 0) ( 0) ( 0)	<50> 2 0 0 0 ( 4) ( 0) ( 0) ( 0)	<50> 2 0 0 0 ( 4) ( 0) ( 0) ( 0)	<50> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)
	hemorrhage	0 ( 0) (	0 0 0 0)(0)(0)	1 0 0 0 (2)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	peliasis-like lesian	0	0 0 0 0)(0)(0)	2 0 0 0 (4)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	necrosis:central	0	2 0 0 4)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	necrosis:focal	1	0 0 0 0)(0)(0)	1 0 0 0 (2)(0)(0)(0)	6 1 0 0 (12)(2)(0)(0)	3 0 0 0 (6)(0)(0)(0)
	fatty change	5 (10)	0 0 0 0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	3 0 0 0 (6)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)
	fatty change:central	0	0 0 0 ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 2) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)

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

STUDY NO.	:	0267
ANIMAL	:	RAT F344/DuCrj
REPORT TYPE	:	A1
SEX	:	FEMALE

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

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)5W)			

Organ	Findings	Group Name Control No. of Animals on Study 50 Grade <u>1 2 3 4</u> (%) (%) (%) (%)	$ \begin{array}{c} 750 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$ \begin{array}{c} 3000 \text{ ppm} \\ 50 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%)  (\%) \end{array} $
[Digestive s	system]				
liver	fatty change:peripheral	$\begin{array}{cccc} <50 > \\ 1 & 0 & 0 & 0 \\ ( 2) & ( 0) & ( 0) & ( 0) \end{array}$	$\langle 50 \rangle$ 1  2  0  0 $( \ 2) \ ( \ 4) \ ( \ 0) \ ( \ 0)$	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)
	inflammatory infiltration	5 0 0 0 (10) (0) (0) (0)	1 1 0 0 (2)(2)(0)(0)	4 0 0 0 (8)(0)(0)(0)	1 0 0 0 ( 2) ( 0) ( 0) ( 0)
	granulation	17 0 0 0 (34) (0) (0) (0)	22 2 0 0 (44)(4)(0)(0)	23 2 0 0 (46)(4)(0)(0)	12 1 0 0 (24)(2)(0)(0)
	extramedullary hematopoiesis	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	clear cell focus	2 0 1 0 ( 4) ( 0) ( 2) ( 0)	2 0 0 0 (4)(0)(0)(0)	2 0 0 0 ( 4) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	acidophilic cell focus	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	basophilic cell focus	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	27 0 0 0 (54) (0) (0) (0)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	28 1 0 0 (56)(2)(0)(0)
	vacuplated cell focus	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	1 0 0 0 (2)(0)(0)(0)	$\begin{pmatrix} 0 & 1 & 0 & 0 \\ ( & 0) & ( & 2) & ( & 0) & ( & 0) \end{pmatrix}$	1 0 0 0 (2) (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 ; \*:  $P \le 0.05$  \*\* :  $P \le 0.01$  Test of Chi Square

STUDY NO.	:	0267
ANIMAL	:	RAT F344/DuCrj
REPORT TYPE	:	A1
SEX	:	FEMALE

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

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0rgan	Findings	Group Name         Control           No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%)	$\begin{array}{c} 750 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$	$ \begin{array}{c} 1500 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
[Digestive s	system]				
liver	mixed cell focus	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 0 0 1 0 ( 0) ( 0) ( 2) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	bile duct hyperplasia	28 1 0 0 (56)(2)(0)(0)	37 0 0 0 (74) (0) (0) (0)	38 0 0 0 (76)(0)(0)(0)	16 0 0 0 * (32) ( 0) ( 0) ( 0)
	biliary cyst	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 2) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
pancreas	atrophy	<pre> &lt;50&gt;     5 2 0 0     ( 10) ( 4) ( 0) ( 0)</pre>	<50> 4 1 0 0 (8) (2) (0) (0)	<50> 3 0 0 0 ( 6) ( 0) ( 0) ( 0)	<50> 3 1 0 0 ( 6) ( 2) ( 0) ( 0)
	inflammation	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
[Urinary sys	stem]				
kidney	infarct	<50> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 3 0 0 0 (6)(0)(0)(0)	<50> 5 0 0 0 (10) (0) (0) (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			

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

(HPT150)

PAGE: 24

STUDY NO.	:	0267
ANIMAL	:	RAT F344/DuCrj
REPORT TYPE	:	A1
SEX	:	FEMALE

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

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PAGE: 25

Organ	:	Group Name Control No. of Animals on Study 50 Grade <u>1 2 3</u> (%) (%) (%)	750 ppm 50 4 (%) 1 2 3 (%) (%) (%)	$\begin{array}{c} 1500 \text{ ppm} \\ 50 \\ \hline 4 \\ \hline (\%) \hline (\%) \\ \hline (\%) \\ \hline (\%) \\ \hline (\%) \hline (\%) \\ \hline (\%) \\ \hline (\%) \hline (\%) \\ \hline (\%) \hline (\%) \\ \hline (\%)$	$ \frac{3000 \text{ ppm}}{50} $
Urinary sy	rstem]				
idney	basophilic change	<50> 0 0 0 ( 0) ( 0) ( 0) (	<50> 0 0 0 0 ( 0) ( 0) ( 0) (	<pre> &lt;50&gt; 0 1 0 0 0 ( 0) ( 2) ( 0) ( 0) ( 0)</pre>	<50> 3 0 0 0 ( 6) ( 0) ( 0) ( 0)
	deposit of hemosiderin	$\begin{pmatrix} 0 & 1 & 0 \\ ( & 0) & ( & 2) & ( & 0) \\ \end{pmatrix}$	0 0 0 0 0) ( 0) ( 0) ( 0) (	0 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0
	deposit of crystal	0 0 0 ( 0) ( 0) ( 0) (	0 0 0 0 0) ( 0) ( 0) ( 0) (	0 1 0 0 0 ( 0) ( 2) ( 0) ( 0) ( 0)	14 3 0 0 * (28) (6) (0) (0)
	inflammatory infiltration	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	0 0 0 0 0) ( 0) ( 0) ( 0) (	0 0 0 0 0 ( 0) ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	chronic nephropathy	15 22 4 (30)(44)(8)(	3 13 28 3 6) (26) (56) (6) (	2 14 25 2 0 ( 4) ( 28) ( 50) ( 4) ( 0)	20 10 0 0 * (40)(20)(0)(0)
	tubular necrosis	0 0 0 ( 0) ( 0) ( 0) (	0 0 0 0 0) ( 0) ( 0) ( 0) (	0 0 0 0 0 ( 0) ( 0) ( 0) ( 0) ( 0)	3 0 0 0 (6)(0)(0)(0)
	papillary necrosis	0 0 0 ( 0) ( 0) ( 0) (	0 4 0 0 0) ( 8) ( 0) ( 0) (	0 13 18 0 0 ( 0) ( 26) ( 36) ( 0) ( 0)	** 10 35 2 0 *: (20)(70)(4)(0)
	mineralization:cortico-medullary juncti	on 300 (6)(0)(0)(	0 0 0 0 0) ( 0) ( 0) ( 0) (	0         0	$\begin{array}{cccccccccccccccccccccccccccccccccccc$

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

b: Number of animals with lesion c: b / a \* 100 b

(c)

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

REPORT TYPE : SEX :	FEMALE					PAGE :
Drgan	Findings	Group Name No. of Animals on Study Grade <u>1</u> (%)	Contral 50 <u>2 3 4</u> (%) (%) (%)		$ \begin{array}{c} 1500 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$ \begin{array}{c} 3000 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $
Urinary syst	rem]					
<idney< td=""><td>mineralization:papilla</td><td>0 ( 0) (</td><td>&lt;50&gt; 0 0 0 0) ( 0) ( 0)</td><td>&lt;50&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</td><td>&lt;50&gt; 6 0 0 0 * (12) (0) (0) (0)</td><td>&lt;50&gt; 19 0 0 0 ** (38) (0) (0) (0)</td></idney<>	mineralization:papilla	0 ( 0) (	<50> 0 0 0 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 6 0 0 0 * (12) (0) (0) (0)	<50> 19 0 0 0 ** (38) (0) (0) (0)
	mineralization:pelvis	7 (14) (	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 (2)(0)(0)(0)
	mineralization:cortex	0 ( 0) (	1 0 0 2)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	3 0 0 0 (6)(0)(0)(0)
	urothelial hyperplasia:pelivis	( 2) (	0 0 0 0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 0 0 0 (4)(0)(0)(0)	24 9 1 0 ** (48) (18) (2) (0)
	eosinophilic droplet:proximal tubule	11 ( 22) (	2 0 0 4) ( 0) ( 0)	14 4 0 0 (28) (8) (0) (0)	24 2 0 0 * (48) (4) (0) (0)	23 0 0 0 * (46)(0)(0)(0)
rin bladd	hemorrhage	0 ( 0) (	<50> 0 0 0 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)
	transitional cell hyperplasia	0 ( 0) (	0 0 0 0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 2) ( 0) ( 0)
Endocrine sy	stem]					
ituitary	tubular structure	( 2) (	<50> 0 0 0 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<49> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)

b b: 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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# HISTOLOCICAL FINDINCS .NON NEODIACTIC LEGIONO (O **DW**

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

)rgan	Findings	Group Name         Control           No. of Animals on Study         50           Grade         1         2         3         4	$\begin{array}{c} 750 \text{ ppm} \\ 50 \\ \hline (\%) \\ (\%$	$ \begin{array}{c} 1500 \text{ ppm} \\ 50 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $	$ \begin{array}{c} 3000 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $
Endocrine sy	'stem]				
ituitary	angiectasis	<50> 12 0 0 0 (24) (0) (0) (0)	<50> 6 1 0 0 (12) (2) (0) (0)	<49> 11 0 0 0 (22) (0) (0) (0)	<50> 16 0 0 0 (32) (0) (0) (0)
	cyst	15 0 0 0 (30) (0) (0) (0)	12 0 0 0 (24) (0) (0) (0)	14 2 0 0 (29)(4)(0)(0)	10 0 0 0 (20)(0)(0)(0)
	deposit of hemosiderin	4 0 0 0 (8)(0)(0)(0)	3 0 0 0 (6)(0)(0)(0)	5 0 0 0 (10) (0) (0) (0)	3 0 0 0 (6)(0)(0)(0)
	hyperplasia	8 3 0 0 (16)(6)(0)(0)	4 3 0 0 (8)(6)(0)(0)	7 2 0 0 (14) (4) (0) (0)	6 2 0 0 (12) (4) (0) (0)
	Rathke pouch	$\begin{array}{ccccc} 7 & 0 & 0 & 0 \\ (14) & (0) & (0) & (0) \end{array}$	5 0 0 0 (10) (0) (0) (0)	8 0 0 0 (16)(0)(0)(0)	9 0 0 0 (18) (0) (0) (0)
yroid	C-cell hyperplasia	<49> 7 2 0 0 (14) (4) (0) (0)	<50> 3 0 0 0 ( 6) ( 0) ( 0) ( 0)	<49> 2 0 0 0 ( 4) ( 0) ( 0) ( 0)	<50> 6 0 0 0 (12) (0) (0) (0)
rathyroid	cyst	<37> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	<38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)

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<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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BAIS3

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

Organ	Findings	Group Name Control No. of Animals on Study 50 Grade <u>1 2 3 4</u> (%) (%) (%) (%)	$\begin{array}{c} 750 \text{ ppm} \\ 50 \\ \hline 1 & 2 & 3 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$	$ \begin{array}{c} 1500 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	3000 ppm 50 <u>1 2 3 4</u> (%) (%) (%) (%
Endocrine s	vstem]				
drenal	hemorrhage	<50> 2 0 0 0 ( 4) ( 0) ( 0) ( 0)	<50> 4 0 0 0 ( 8) ( 0) ( 0) ( 0)	<50> 3 0 0 0 ( 6) ( 0) ( 0) ( 0)	<50> 8 1 0 0 (16) (2) (0) (0)
	peliosis-like lesion	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	22 12 0 0 (44)(24)(0)(0)	22 8 1 0 (44)(16)(2)(0)	15 21 0 0 (30)(42)(0)(0)
	cyst	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 2) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	extramedullary hematopoiesis	0 1 0 0 ( 0) ( 2) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 0 0 0 ( 4) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	hyperplasia:cortical cell	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	2 0 0 0 (4)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	hyperplasia:medulla	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	0 0 0 0 (0)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)	0 1 0 0 ( 0) ( 2) ( 0) ( 0)
	focal fatty change:cortex	5 0 0 0 (10) (0) (0) (0)	4 0 0 0 (8)(0)(0)(0)	7 0 0 0 (14)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
Reproductive	» system]				
Jary	cyst	<49> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 3 0 0 0 ( 6) ( 0) ( 0) ( 0)	<50> 4 0 0 0 ( 8) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)

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

(HPT150)

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

PAGE : 29

Drgan	Findings	Group Name         Control           No. of Animals on Study         50           Grade         1         2         3         4	$ \begin{array}{c} 750 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$ \begin{array}{c} 1500 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$\begin{array}{c} 3000 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$
Reproductive	system]				
iterus	dilatation	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 2 0 0 0 ( 4) ( 0) ( 0) ( 0)	<50> 0 1 0 0 ( 0) ( 2) ( 0) ( 0)
	cell debris	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)	0 1 0 0 ( 0) ( 2) ( 0) ( 0)
	cystic endometrial hyperplasia	3 4 0 0 (6)(8)(0)(0)	3 3 1 0 (6)(6)(2)(0)	6 0 0 0 (12) (0) (0) (0)	7 2 1 0 (14) (4) (2) (0)
ammary gl	duct ectasia	$\begin{array}{cccc} <50> & & \\ 1 & 0 & 0 & 0 \\ ( 2) & ( 0) & ( 0) & ( 0) \end{array}$	<50> 0 1 0 0 ( 0) ( 2) ( 0) ( 0)	<50> 4 0 0 0 ( 8) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	abscess	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 2) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	hyperplasia	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 0 0 0 (4)(0)(0)(0)	2 0 0 0 ( 4) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	salactocele	4 2 0 0 (8)(4)(0)(0)	9 0 0 0 (18)(0)(0)(0)	3 0 0 0 (6)(0)(0)(0)	3 0 0 0 (6)(0)(0)(0)
Special sense	organs/appandage]				
/8	gliosis	<50> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)

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

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

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PAGE: 30

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0rgan	Findings	Group Name Control No. of Animals on Study 50 Grade <u>1 2 3 4</u> (%) (%) (%) (%)	$\begin{array}{c} 750 \text{ ppm} \\ 50 \\ \hline (\%) \\ (\%$	1500 ppm 50 <u>1 2 3 4</u> (%) (%) (%) (%)	$ \begin{array}{c} 3000 \text{ ppm} \\ 50 \\ \frac{1}{(\%)}  (\%)  (\%)  (\%)  (\%) \end{array} $
[Special sen	se organs/appandage]				
еуе	cataract	$\begin{array}{c} <50>\\ 1 & 0 & 0 & 0\\ ( 2) & ( 0) & ( 0) & ( 0) \end{array}$	<50> 3 0 0 0 (6)(0)(0)(0)	<50> 3 0 0 0 ( 6) ( 0) ( 0) ( 0)	<50> 2 0 0 0 ( 4) ( 0) ( 0) ( 0)
	retinal atrophy	5 0 1 0 (10) (0) (2) (0)	0 1 2 0 ( 0) ( 2) ( 4) ( 0)	4 3 0 0 (8)(6)(0)(0)	5 0 0 0 (10)(0)(0)(0)
	keratitis	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	deseneration:cornea	$\begin{pmatrix} 1 & 0 & 0 & 0 \\ ( & 2) & ( & 0) & ( & 0) & ( & 0) \end{pmatrix}$	2 0 0 0 (4)(0)(0)(0)	2 0 0 0 (4)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	Vascularization:cornea	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	1 0 0 0 (2)(0)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
larder gl	granulation	<50> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)
asolacr d	inflammation	<50> 6 0 0 0 (12) (0) (0) (0)	<50> 8 0 0 0 ( 16) ( 0) ( 0) ( 0)	<50> 4 0 0 0 ( 8) ( 0) ( 0) ( 0)	<50> 11 0 0 0 (22) (0) (0) (0)

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

(HPT150)

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

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Organ	Findings	Group Name Control No. of Animals on Study 50 Grade <u>1 2 3</u> (%) (%) (%)	$     \frac{4}{(\%)}  \frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}  \frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}  \frac{1}{(\%)}  \frac{2}{(\%)}  \frac{4}{(\%)}  \frac{1}{(\%)}  \frac{1}{(\%)} $	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
Musculoskel	ətal system]				
uscle	necrosis:focal	<50> 0 0 0 ( 0) ( 0) ( 0) (	$\begin{array}{cccc} & <50 \\ 0 & 1 & 0 & 0 \\ 0 & (2) & (0) & (0) & (0) \end{array}$	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
ane	fracture	<50> 0 0 0 ( 0) ( 0) ( 0) (	<50> 0 0 0 0 0 0) ( 0) ( 0) ( 0) ( 0)	<50> 0 1 0 0 ( 0) ( 2) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	osteosclerosis	4 4 1 ( 8) ( 8) ( 2) (	0 10 3 1 0 0) (20) (6) (2) (0)	8 5 2 0 (16)(10)(4)(0)	5 7 6 0 (10) (14) (12) (0)
articulus	ossification	<50> 0 0 0 ( 0) ( 0) ( 0) ( 1	<50> 0 0 0 0 0 0) ( 0) ( 0) ( 0) ( 0)	<50> 0 1 0 0 ( 0) ( 2) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
ody cavitie	s]				
ritoneum	peritonitis	<50> 0 0 0 ( ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 0) ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 0 1 0 0 ( 0) ( 2) ( 0) ( 0)
lipose	granulation	<50> 1 0 0 ( ( 2) ( 0) ( 0) ( 0)	<50> 0 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<50> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)

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

(HPT150)

# APPENDIX L 5

# HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

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

(2-YEAR STUDY)

STUDY NO.	:	0267
ANIMAL	:	RAT F344/DuCrj
REPORT TYPE	:	A1
SEX	:	FEMALE

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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					PAGE :
)rgan	Findings	Group Name     Control       No. of Animals on Study     12       Grade     1     2     3     4       (%)     (%)     (%)     (%)     (%)	$\begin{array}{c} 750 \text{ ppm} \\ 9 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$	$ \begin{array}{c} 1500 \text{ ppm} \\ 8 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
Integumentar	y system/appandage]				
skin/app	ulcer	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<11> 1 0 0 0 ( 9) ( 0) ( 0) ( 0)
[Respiratory :	system]				
nasal cavit	ulcər	$\begin{array}{c} <12 \\ 1 & 0 & 0 & 0 \\ (8) & (0) & (0) & (0) \end{array}$	<pre> &lt; 9&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>	<pre> &lt; 8&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>	<11> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	mineralization	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 (9)(0)(0)(0)(0)
	inflammation	0 1 0 0 ( 0) ( 8) ( 0) ( 0)	0 0 0 0 (0)(0)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (9)(0)(0)(0)
	hyperplasia:gland	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (11)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	goblet cell hyperplasia	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 (0)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (9)(0)(0)(0)(0)
	eosinophilic change:olfactory epithel	.ium 9000 (75)(0)(0)(0)	6 0 0 0 (67)(0)(0)(0)	7 0 0 0 (88) (0) (0) (0)	7 0 0 0 (64)(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) DEAD AND MORIBUND ANIMALS (0-1059)

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Organ	Ne	roup Name Control 5. of Animals on Study 12 rade <u>1 2 3 4</u> (%) (%) (%) (%)	$ \begin{array}{c} 750 \text{ ppm} \\ 9 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$ \begin{array}{c} 3000 \text{ ppm} \\ 11 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $
Respiratory	system]				
nasal cauit	eosinophilic change:respiratory epithel	<12> ium 1 0 0 0 ( 8) ( 0) ( 0) ( 0)	< 9> 1 0 0 0 (11) (0) (0) (0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<11> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	inflammation:foreign body .	$\begin{pmatrix} 1 & 0 & 0 & 0 \\ (8) & (0) & (0) & (0) \end{pmatrix}$	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (13) (0) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	respiratory metaplasia:gland	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 0 0 0 (25)(0)(0)(0)	3 0 0 0 (27)(0)(0)(0)
	squamous cell metaplasia:respiratory ep	ithelium 1 0 0 0 (8)(0)(0)(0)	1 0 0 0 (11) (0) (0) (0)	0 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (9)(0)(0)(0)
агулх	ulcer	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<11> 1 0 0 0 ( 9) ( 0) ( 0) ( 0)
lung	congestion	$\begin{array}{cccc} & & <12 \\ & 4 & 0 & 0 & 0 \\ ( 33 ) & ( & 0 ) & ( & 0 ) & ( & 0 ) \end{array}$	< 9> 2 0 0 0 ( 22) ( 0) ( 0) ( 0)	< 8> 3 0 0 0 ( 38) ( 0) ( 0) ( 0)	<11> 3 0 0 0 ( 27) ( 0) ( 0) ( 0)
	deposit of hemosiderin	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)

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

b b: Number of animals with lesion

(c) c:b/a\*100

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

		Group Name Control No. of Animals on Study 12 Grade 1 2 3 4	750 ppm 9 1 2 3 4	1500 ppm 8 1 2 3 4	3000 ppm 11 1 2 3 4
gan	Findings		$\frac{1}{(\%)}$ $\frac{2}{(\%)}$ $\frac{3}{(\%)}$ $\frac{3}{(\%)}$	$\frac{1}{(\%)}$ $\frac{2}{(\%)}$ $\frac{3}{(\%)}$ $\frac{4}{(\%)}$	$\frac{1}{(\%)}$ $\frac{2}{(\%)}$ $\frac{3}{(\%)}$ $\frac{4}{(\%)}$
spiratory	v system]				
ng	granulation	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<11> 1 0 0 0 ( 9) ( 0) ( 0) ( 0
	accumulation of foamy cells	0 0 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 (9)(0)(0)(0)
ematopoie	tic system]				
ne marrow	congestion	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre> &lt; 9&gt; 1 0 0 0 ( 11) ( 0) ( 0) ( 0) </pre>	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<11> 2 0 0 0 ( 18) ( 0) ( 0) ( 0
	hemorrhage	2 0 0 0 (17) (0) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	3 0 0 0 (27)(0)(0)(0)
	decreased hematopoiesis	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (11)(0)(0)(0)	0 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (9)(0)(0)(0)
	erythropoiesis:increased	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (13)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0
leen	deposit of hemosiderin	$\begin{array}{c} <12>\\ 5 & 1 & 0 & 0\\ (42) & (8) & (0) & (0)\end{array}$	< 9> 1 3 0 0 (11) (33) (0) (0)	< 8> 3 0 0 0 ( 38) ( 0) ( 0) ( 0)	<11> 3 4 0 0 ( 27) ( 36) ( 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

# BAIS3

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

	• • • • • • • • • • • • • • • • • • •				PAGE : 14
0rgan	Findings	Group Name Control No. of Animals on Study 12 Grade <u>1 2 3 4</u> (%) (%) (%) (%)	$     \begin{array}{r}       750 \text{ ppm} \\       9 \\       \frac{1  2  3  4}{(\%)  (\%)  (\%)  (\%)}     \end{array} $	$     1500 \text{ ppm} \\     8 \\     1 2 3 4 \\     (\%) (\%) (\%) (\%) (\%)   $	$\begin{array}{c} 3000 \text{ ppm} \\ 11 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array}$
[Hematopoie	otic system]				
spleen	fibrosis	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<11> 1 1 0 0 ( 9) ( 9) ( 0) ( 0)
	extramedullary hematopoiesis	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	0 1 0 0 ( 0) ( 11) ( 0) ( 0)	3 0 0 0 (38)(0)(0)(0)	1 0 0 0 (9)(0)(0)(0)(0)
[Circulator	y system]				
heart	thrambus	<12> 1 0 0 0 ( 8) ( 0) ( 0) ( 0)	< 9> 0 1 0 0 ( 0) ( 11) ( 0) ( 0)	< 8> 1 0 0 0 (13) (0) (0) (0)	<11> 0 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	necrosis:focal	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 (0)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 3 0 ( 0) ( 0) ( 27) ( 0)
	mineralization	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	myocardial fibrosis	$\begin{array}{ccccc} 6 & 1 & 0 & 0 \\ (50) & (8) & (0) & (0) \end{array}$	1 1 0 0 (11)(11)(0)(0)	1 0 0 0 (13) (0) (0) (0)	4 1 0 0 (36)(9)(0)(0)
	endocarditis	0 1 0 0 ( 0) ( 8) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (13) (0) (0) (0)	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</a>

b b: Number of animals with lesion

(c) c:b/a\*100

STUDY NO. : 0267

REPORT TYPE : A1

ANIMAL

SEX

: RAT F344/DuCrj

: FEMALE

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

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#### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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rgan	Findings	Group Name No. of Animals on Study Grade <u>1</u> (%)	Control 12 2 3 4 (%) (%) (%)	750 ppm 9 <u>1 2 3 4</u> (%) (%) (%) (%)	1500 ppm 8 <u>1 2 3 4</u> (%) (%) (%) (%)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
Digestive sys	stem]					
ral cavity	ulcer	0 ( 0) (	<12> 0 0 0 ( 0) ( 0) ( 0)	<pre> &lt; 9&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0) </pre>	< 8> 1 0 0 0 (13) (0) (0) (0)	$\begin{array}{c} <11>\\ 1 & 0 & 0 & 0\\ (9) & (0) & (0) & (0) \end{array}$
tomach	mineralization	0 ( 0) (	<12> 1 0 0 ( 8) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<11> 1 0 0 0 ( 9) ( 0) ( 0) ( 0)
	ulcer:forestomach	0 ( 0)	0 2 0 ( 0) ( 17) ( 0)	1 1 1 1 (11) (11) (11) (11)	1 0 0 0 (13) (0) (0) (0)	1 0 0 Ó (9)(0)(0)(0)
	hyperplasia:forestomach	1 ( 8)	2 0 0 (17) (0) (0)	1 0 0 0 (11) (0) (0) (0)	1 0 0 0 (13) (0) (0) (0)	0 2 0 0 ( 0) (18) ( 0) ( 0)
	erosion:glandular stomach	0 ( 0)	0 0 0 ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 11) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 ( 9) ( 0) ( 0) ( 0)
	ulcer:glandular stomach	1	1 0 0 ( 8) ( 0) ( 0)	1 0 0 0 (11) (0) (0) (0)	1 1 0 0 (13)(13)(0)(0)	1 0 0 0 ( 3) ( 0) ( 0) ( 0)
i∪er	herniation	1	<12> 0 0 0 ( 0) ( 0) ( 0)	<pre> &lt; 9&gt;     1 0 0 0     (11) (0) (0) (0) </pre>	< 8> 1 0 0 0 (13) (0) (0) (0)	<11> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)

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

b : Number of animals with lesion b

c:b/a\*100 (c)

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

(HPT150)

#### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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PAGE : 16

Drgan	Findings	Group Name         Control           No. of Animals on Study         12           Grade         1         2         3           (%)         (%)         (%)         (%)	$ \frac{4}{\cancel{5}} \qquad \frac{1 \ 2 \ 3 \ 4}{\cancel{5}} \qquad \frac{1 \ (\cancel{5}) \ (\cancel{5}) \ (\cancel{5}) \ (\cancel{5})}{\cancel{5}} $	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{c} 3000 \text{ ppm} \\ 11 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$
[Digestive :	system]				
liver	necrosis:central	<12> 0 2 0 ( 0) ( 17) ( 0) (	0 0 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<11> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	necrosis:focal	0 0 0 ( 0) ( 0) ( 0) (	0 0 0 0 0 0) ( 0) ( 0) ( 0) ( 0)	2 1 0 0 (25)(13)(0)(0)	1 0 0 0 (9)(0)(0)(0)
~	fatty change	2 0 0 (17)(0)(0)(	0 0 0 0 0 0) ( 0) ( 0) ( 0) ( 0)	2 0 0 0 (25)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	fatty change:central	0 0 0 ( 0) ( 0) ( 0) (	0 0 1 0 0 0) ( 0) ( 11) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
fatty change	fatty change:peripheral	1 0 0 (8)(0)(0)(	0 0 2 0 0 0) ( 0) ( 22) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	granulation	1 0 0 ( 8) ( 0) ( 0) (	0 2 0 0 0 0) (22) (0) (0) (0)	3 0 0 0 (38)(0)(0)(0)	1 0 0 0 (9)(0)(0)(0)(0)
	acidophilic cell focus	0 0 0 ( 0) ( 0) ( 0) (	0 0 0 0 0 0) ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (13)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	basophilic cell focus	2 0 0 (17) (0) (0) (	0 1 0 0 0 0) (11) (0) (0) (0)	1 0 0 0 (13) (0) (0) (0)	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 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

)	Findings	Group Name Control No. of Animals on Study 12 Grade <u>1 2 3 4</u> (%) (%) (%) (%)	$\begin{array}{c} 750 \text{ ppm} \\ 9 \\ \frac{1}{(\%)} (\%) (\%) (\%) (\%) (\%) \end{array}$	1500  ppm 8 $\frac{1}{2} \frac{2}{3} \frac{3}{4}$	$ \begin{array}{c} 3000 \text{ ppm} \\ 11 \\ \underline{1 \ 2 \ 3 \ 4} \\ (0) \ (0) \ (0) \ (0) \end{array} $
Organ	rinaings		(%) (%) (%)	(%) (%) (%)	(%) (%) (%) (%)
Digestive sy	stem]				
liver	vacuolated cell focus	$\begin{pmatrix} <12 > \\ 0 & 1 & 0 & 0 \\ ( & 0) & ( & 8) & ( & 0) & ( & 0) \end{pmatrix}$	<pre> &lt; 9&gt; 0 0 0 0 0 ( 0) ( 0) ( 0) ( 0) ( 0)</pre>	<pre> &lt; 8&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>	<11> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	bile duct hyperplasia	3 0 0 0 (25)(0)(0)(0)	7 0 0 0 (78)(0)(0)(0)	4 0 0 0 (50)(0)(0)(0)	2 0 0 0 (18) (0) (0) (0)
	biliary cyst	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 11) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
pancreas	atrophy	$\begin{array}{c} <12>\\ 2 & 0 & 0 & 0\\ (17) & (0) & (0) & (0) \end{array}$	<pre> &lt; 9&gt; 0 0 0 0   ( 0) ( 0) ( 0) ( 0) ( 0)</pre>	<pre></pre>	<11> 1 0 0 0 ( 9) ( 0) ( 0) ( 0)
	inflammation	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (11) (0) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
[Urinary syst	em]				
kidney	deposit of crystal	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<11> 2 1 0 0 (18) (9) (0) (0)

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(HPT150)

BAIS3

0rgan	Findings	Group Name         Control           No. of Animals on Study         12           Grade         1         2         3         4           (%)         (%)         (%)         (%)	$\begin{array}{c} 750 \text{ ppm} \\ 9 \\ \hline (\%) (\%) (\%) (\%) (\%) \\ (\%) (\%) (\%) \end{array}$	1500 ppm 8 <u>1 2 3 4</u> (%) (%) (%) (%)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
(Urinary syst	tem]				
kidney ,	chronic nephropathy	$\begin{array}{c} <12 > \\ 3 & 2 & 1 & 2 \\ (25) & (17) & (8) & (17) \end{array}$	< 9> 2 2 1 1 (22) (22) (11) (11)	< 8> 1 5 0 0 (13) (63) (0) (0)	<11> 2 1 0 0 ( 18) ( 9) ( 0) ( 0)
	tubular necrosis	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	3 0 0 0 (27) (0) (0) (0)
	papillary necrosis	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	3 2 0 0 ** (38) (25) (0) (0)	3 7 1 0 ** (27) (64) (9) (0)
	mineralization:papilla	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (13) (0) (0) (0)	6 0 0 0 * (55)(0)(0)(0)
	mineralization:pelvis	3 0 0 0 (25)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	mineralization:cortex	$\begin{pmatrix} 0 & 1 & 0 & 0 \\ ( & 0) & ( & 8) & ( & 0) & ( & 0) \end{pmatrix}$	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	3 0 0 0 (27)(0)(0)(0)
	urothelial hyperplasia:pelivis	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	4 1 1 0 * (36) (9) (9) (0)
	eosinophilic droplet:proximal tubu	Le 2 0 0 0 (17)(0)(0)(0)	2 2 0 0 (22)(22)(0)(0)	1 0 0 0 (13) (0) (0) (0)	2 0 0 0 (18) (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

STUDY NO. : 0267

REPORT TYPE : A1

: RAT F344/DuCrj

: FEMALE

ANIMAL

SEX

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

#### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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PAGE: 18

BAIS3

rgan	Findings	Group Name Control No. of Animals on Study 12 Grade <u>1 2 3 4</u> (%) (%) (%)	$\begin{array}{c} 750 \text{ ppm} \\ 9 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
Urinary syst	rem]				
rin bladd	hemorrhage	$\begin{pmatrix} <12> \\ 0 & 0 & 0 \\ ( & 0) & ( & 0) & ( & 0) \\ \end{pmatrix}$	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<11> 1 0 0 0 ( 9) ( 0) ( 0) ( 0)
Endocrine sy	/stem]				
ituitary	angiectasis	$\begin{array}{c} <12>\\ 1 & 0 & 0 & 0\\ (8) & (0) & (0) & (0) \end{array}$	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<11> 3 0 0 0 ( 27) ( 0) ( 0) ( 0)
	cyst	2 0 0 0 (17) (0) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 13) ( 0) ( 0)	
	deposit of hemosiderin	1 0 0 0 ( 8) ( 0) ( 0) ( 0)	1 0 0 0 (11)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	Rathke pouch	1 0 0 0 ( 8) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
hyroid	C-cell hyperplasia	<11> 1 0 0 0 ( 9) ( 0) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>	$\langle 11 \rangle$ 0 0 0 0 ( 0) ( 0) ( 0) ( 0)

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

(HPT150)

BAIS3

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

)rgan	N	roup Name Control o. of Animals on Study 12 rade <u>1 2 3 4</u> (%) (%) (%) (%)	$\begin{array}{c} 750 \text{ ppm} \\ 9 \\ \underline{1  2  3  4} \\ (\cancel{x})  (\cancel{x})  (\cancel{x})  (\cancel{x}) \end{array}$	$ \begin{array}{c} 1500 \text{ ppm} \\ 8 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $	$\begin{array}{c} 3000 \text{ ppm} \\ 11 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$
Endocrine	system]				
drenal	hemorrhage	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<11> 2 0 0 0 (18) (0) (0) (0)
	peliosis-like lesion	0 3 0 0 ( 0) ( 25) ( 0) ( 0)	1 2 0 0 (11)(22)(0)(0)	1 2 0 0 (13)(25)(0)(0)	2 1 0 0 (18) (9) (0) (0)
	extramedullary hematopoiesis	0 1 0 0 ( 0) ( 8) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	focal fatty change:cortex	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (11)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
Reproducti	ue system]				
Jary	cyst	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 9> 1 0 0 0 (11) (0) (0) (0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<11> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
terus	cystic endometrial hyperplasia	$\begin{array}{c} <12>\\ 1 & 1 & 0 & 0\\ ( 8) & ( 8) & ( 0) & ( 0) \end{array}$	< 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<11> 1 1 0 0 ( 9) ( 9) ( 0) ( 0)
rade 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 e			

(HPT150)

BAIS3

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

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#### STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE Group Name No. of Animals on Study Grade 0rgan\_ Findings\_

#### fn ......

[Reproductive	system]			
mammary gl	duct ectasia	<12>     < 9>       0     0     0     0     0       (0)     (0)     (0)     (0)     (0)     (0)	< 8> 1 0 0 0 (13) (0) (0) (0) ()	<11> 0 0 0 0 0) ( 0) ( 0) ( 0)
	abscess	0 0 0 0 0 0 1 0 0 ( 0) ( 0) ( 0) ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0) (	0 0 0 0 0)(0)(0)(0)(0)
	hyperplasia	0       0       0       0       2       0       0       0         (       0)       (       0)       (       0)       (       22)       (       0)       (       0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0) (	0 0 0 0 0)(0)(0)(0)
	galactocele	1       1       0       0       4       0       0       0         (8)       (8)       (0)       (0)       (44)       (0)       (0)       (0)	1 0 0 0 (13)(0)(0)(0)(0)(	1 0 0 0 9)(0)(0)(0)(0)
[Special sense	organs/appandago]			
еуе	gliosis	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0) (	<11> 0 0 0 0 0) ( 0) ( 0) ( 0)

cataract 0 0 0 0 0 0 0 0 (0)(0)(0)(0) ( 0) ( 0) ( 0) ( 0) retinal atrophy 0 0 0 0 0 0 0 0

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

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

ь 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) DEAD AND MORIBUND ANIMALS (0-105W)

750 ppm

3

(%) (%)

4

9

2

(%)

(%)

1500 ppm

3

(%)

4

(%)

8

1 0 0 0

(13) (0) (0) (0)

1 0 0 0

(13) (0) (0) (0)

2

(%)

(%)

Control

3

(%) (%)

4

12

2

(%)

(%)

PAGE : 21

4

3000 ppm

11

0 0 0 0

(0)(0)(0)(0)

1 0 0 0

(9)(0)(0)(0)

2 3

(%) (%) (%)

(%)

BAIS3

)rgan	Findings	Group Name         Control           No. of Animals on Study         12           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%)	$\begin{array}{c} 750 \text{ ppm} \\ 9 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$ \begin{array}{c} 3000 \text{ ppm} \\ 11 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $
Special sens	e organs/appandage]				
уе	keratitis	$\begin{array}{c} <12 \\ 0 & 1 & 0 & 0 \\ ( & 0) & ( & 8) & ( & 0) & ( & 0) \end{array}$	<pre></pre>	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<11> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
asolaor d	inflammation	$\begin{array}{c} <12>\\ 1 & 0 & 0 & 0\\ (8) & (0) & (0) & (0)\end{array}$	<pre> &lt; 9&gt;     1 0 0 0     ( 11) ( 0) ( 0) ( 0)</pre>	< 8> 1 0 0 0 (13) (0) (0) (0)	<11> 1 0 0 0 ( 9) ( 0) ( 0) ( 0)
Musculoskele	otal system]				
uscle	necrosis:focal	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	$\begin{array}{cccc} & \langle 9 \rangle \\ 1 & 0 & 0 & 0 \\ (11) & (0) & (0) & (0) \end{array}$	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>
ene	asteasclerasis	$\begin{array}{c} <12 \\ 2 & 0 & 0 & 0 \\ (17) & (0) & (0) & (0) \end{array}$	<pre> &lt; 9&gt; 3 0 0 0 (33) (0) (0) (0)</pre>	< 8> 0 1 1 0 ( 0) ( 13) ( 13) ( 0)	<11> 1 0 2 0 ( 9) ( 0) ( 18) ( 0)

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(HPT150)

BAIS3

# APPENDIX L 6

# HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

# HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

Group Name       Control       750 ppm         No. of Animals on Study       38       41         Grade       1       2       3       4         Organ       Findings       (%)       (%)       (%)       (%)       (%)         [Integumentary system/appandage]       Integrandage]       Integrandage       Integrandage       Integrandage       Integrandage       Integrandage	$ \begin{array}{c} 1500 \text{ ppm} \\ 42 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $	3000 ppm 39 <u>1 2 3 4</u> (%) (%) (%) (%)
kin/app     <38>     <41>       ulcer     0     0     0     0     0       (0)     (0)     (0)     (0)     (0)     (0)     (0)	<42> 5 0 0 0 (12) (0) (0) (0)	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
squamous cell hyperplasia 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2 0 0 0 (5)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
espiratory system]		
Isal cavit     <38>     <41>       hemorrhage     0     0     0     0     0       (0)     (0)     (0)     (0)     (0)     (0)     (0)	<42> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
mineralization 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	1 0 0 0 (2)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
inflammation 2 1 0 0 1 0 0 0 (5) (3) (0) (2) (0) (0)	3 0 0 0 (7)(0)(0)(0)	1 0 0 0 (3)(0)(0)(0)(0)
hyperplasia:gland 0 0 0 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 (3)(0)(0)(0)(0)
goblet cell hyperplasia800700(21)(0)(0)(17)(0)(0)(0)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	3 1 0 0 (8)(3)(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 ; \*:  $P \le 0.05$  \*\*:  $P \le 0.01$  Test of Chi Square

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#### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

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Organ	Findings	Group Name No. of Animals on Study Grade <u>1</u> (%)	Contral 38 <u>2 3</u> (%) (%)	<u>4</u> <u>1</u> (%) (%)	4 2	3	<u>4</u> (%)	<u>1</u> (%)	1500 p 42 2 3 (%) (%	4	<u>1</u> (%) (	3000 ppm 39 <u>2 3</u> %) (%)	<u>4</u> (%)
[Respiratory	system]												
nasal cavit	eosinophilic change∶olfactory epithel		<38> 2 0 ( 5) ( 0) (	0 39 0) (95	1	1> 0 ( 0) (	0)	38 (90) (	<42> 4 0 10) ( 0		22 1 (56)(4		0 ** ( 0)
luns	eosinophilic change:respiratory epith	əlium 2 (5)	0 0 ( 0) ( 0) (	0 13 0) (32	0 ) ( 0)	0 ( 0) (	0 ** 0)	13 (31) (	0 0 0) ( 0	0 ** ) ( 0)	8 (21) (	0 0 0)(0)	0 ( 0)
	inflammation:foreign body	2 ( 5)	0 0 ( 0) ( 0) (	0 3 0) (7	0 ) ( 0)	0 ( 0) (	0 0)	3 (7)(	0 0 0)(0	0 ) ( 0)	4 (10) (	0 0 0)(0)	
	respiratory metaplasia:gland	9 (24)	0 0 ( 0) ( 0) (	0 11 0) (27		0 ( 0) (	0 0)	14 (33) (	0 0 0)(0	0 ) ( 0)	12 (31) (	0 0 0)(0)	0 ( 0)
	squamous cell metaplasia:respiratory	epithelium 2 (5)	0 0 (	0 1 0) (2	0 ) ( 0)	0(0)(	0 0) .	3 (7)(	0 0 0)(0	0 ) ( 0)	1 (3)(	0 0 0)(0)	0 ( 0)
	hemorrhage	4 (11)	<38> 0 0 ( 0) ( 0) (	0 1 0) ( 2	0	1> 0 ( 0) (	0 0)	0 ( 0) (	<42> 0 0 0) ( 0		0 ( 0) (	<39> 0 0 0) ( 0)	0 ( 0)
	granulation	0 ( 0)	0 0 ( 0) ( 0) (	0 ( 0) ( 0		0 ( 0) (	0 0)	2 (5)(	0 0 0) ( 0	0 ) ( 0)	1 ( 3) (	0 0 0)(0)	0 ( 0)
	accumulation of foamy cells	2 ( 5)	0 0 ( 0) ( 0) (	0 3 0) (7	) ( 0)	0 ( 0) (	0 0)	5 (12) (	0 0 0) ( 0	0 ) ( 0)	13 (33) (	1 0 3)(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

n - F - Fit sol		Group Name	Control	750 ppm	1500 ppm	3000 ppm		
rgan	Findings	No. of Animals on Study Grade <u>1</u> (%)	38 <u>2 3 4</u> (%) (%) (%)	$\begin{array}{cccc} & 41 \\ \underline{1 & 2 & 3 & 4} \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$	$\begin{array}{c} 42 \\ \underline{1  2  3  4} \\ \hline (\%)  (\%)  (\%)  (\%) \\ \hline (\%) \\ \end{array}$	$     \frac{1 2 3 4}{(\%) (\%) (\%) (\%) (\%)} $		
espiratory	system]							
ng	bronchiolar-alveolar cell hyperplasia		<38> 1 0 0 ( 3) ( 0) ( 0)	<41> 0 2 0 0 ( 0) ( 5) ( 0) ( 0)	<42> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)		
lematopoieti	c system]							
ne marrow	congestion	1 ( 3)	<38> 0 0 0 ( 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<42> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<39> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)		
	hemorrhage	1 ( 3)	0 0 0 0 ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)		
	granulation	2 (5)	0 0 0 ( 0) ( 0) ( 0)	3 0 0 0 (7)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	4 0 0 0 (10) (0) (0) (0)		
	decreased 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)	1 0 0 0 (3)(0)(0)(0)		
	erythropoiesis:increased	2 ( 5)	0 0 0 ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)(0)	1 0 0 0 (2) (0) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)		
mph node	ectopic tissue	0 ( 0)	<38> 0 0 0 ( 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<42> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<39> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)		

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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

STUDY NO.	:	0267
ANIMAL.	:	RAT F344/DuCrj
REPORT TYPE	:	A1
SEX	:	FEMALE

# HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

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		Group Name Control No. of Animals on Study 38	750 ppm 41	1500 ppm 42	3000 maa 39	
Drgan	Findings	Grade <u>1 2 3 4</u> (%) (%) (%) (%)		$\frac{1  2  3  4}{(\%)  (\%)  (\%)  (\%)}$	$\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$	
[Hematopoiet	ic system]					
spleen	congestion	<pre>&lt;38&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>		<42> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	$\langle 39 \rangle$ 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	
	hemorrhage	$\begin{array}{cccccccccccccccccccccccccccccccccccc$		0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	
	deposit of hemosiderin	29 0 0 0 (76)(0)(0)(0)		24 0 0 0 (57)(0)(0)(0)	15 0 0 0 ** (38) (0) (0) (0)	
	extramedullary hematopoiesis	12 2 0 0 (32)(5)(0)(0		11 1 0 0 (26)(2)(0)(0)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
[Circulatory	/ system]					
heart	myocardial fibrosis	<38> 11 0 0 0 (29) (0) (0) (0		<42> 14 0 0 0 (33) (0) (0) (0)	<39> 9 0 0 0 (23) (0) (0) (0)	
[Digestive s	system]					
tooth	inflammation	<38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0		<42> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	
Grade < 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 site				

Organ\_

stomach

large intes

Liver

#### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

Group Name Control 750 ppm 1500 ppm 3000 ppm No. of Animals on Study 38 41 42 39 Grade 2 3 4 2 3 2 3 2 3 4 4 Findings (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) [Digestive system] <38> <41> <42> <39> ulcer:forestomach 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 (0)(0)(0)(0) ( 0) ( 0) ( 0) ( 0) (2) (0) (0) (0) (0)(0)(0)(0)hyperplasia:forestomach 0 0 0 0 0 0 0 0 3 0 0 0 0 0 0 0 (0)(0)(0)(0)(0)(0)(0)(0) (7) (0) (0) (0) (0)(0)(0)(0)erosion:glandular stomach 1 0 0 0 1 0 0 0 2 0 0 0 0 0 0 0 (3) (0) (0) (0) (2) (0) (0) (0) (5) (0) (0) (0)(0)(0)(0)(0) ulcer:glandular stomach 0 0 0 0 1 0 0 0 0 0 0 - 0 1 0 0 0 (0)(0)(0)(0)(2) (0) (0) (0) (0)(0)(0)(0) (3)(0)(0)(0) <38> <41> <42> <39> mineralization 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 (3) (0) (0) (0) (0)(0)(0)(0)(0)(0)(0)(0) <38> **<41>** <42> <39> herniation 0 4 0 0 1 0 0 0 0 0 0 0 0 1 0 1 (11) (0) (0) (0) (2) (0) (0) (0) (2) (0) (0) (0) (3)(0)(0)(0) hemorrhage 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0)(2)(0)(0)(0)

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

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

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

(0)(0)(0)(0)

(0)(0)(0)(0)

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

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PAGE : 20

)rgan	Findings	Group NameControlNo. of Animals on Study38Grade $\frac{1}{(\%)}$ $\frac{2}{(\%)}$ $\frac{3}{(\%)}$	$\begin{array}{c} 750 \text{ ppm} \\ 41 \\ \underline{1  2  3  4} \\ \hline (\%)  (\%)  (\%)  (\%) \end{array}$	$\begin{array}{c} 1500 \text{ ppm} \\ 42 \\ \underline{1} & \underline{2} & \underline{3} & \underline{4} \\ (\%) & (\%) & (\%) & (\%) \end{array}$	. 3000 ppm 39 <u>1 2 3 4</u> (%) (%) (%) (%)
(Digestive s	system]				
liver	peliosis-like lesion	<38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre> &lt;41&gt;     2 0 0 0     ( 5) ( 0) ( 0) ( 0)</pre>	<42> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	necrosis:focal	1 0 0 0 (3)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)(0)	4 0 0 0 (10) (0) (0) (0)	2 0 0 0 (5)(0)(0)(0)
	fatty change	3 0 0 0 (8)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)	1 0 0 0 (3)(0)(0)(0)
	fatty change:peripheral	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (3)(0)(0)(0)
	inflammatory infiltration	5 0 0 0 (13) (0) (0) (0)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	4 0 0 0 (10) (0) (0) (0)	1 0 0 0 (3)(0)(0)(0)
	granulation	16 0 0 0 (42) (0) (0) (0)	20 2 0 0 (49)(5)(0)(0)	20 2 0 0 (48)(5)(0)(0)	11 1 0 0 (28) (3) (0) (0)
	extramedullary hematopoiesis	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	clear cell focus	$\begin{pmatrix} 2 & 0 & 1 & 0 \\ (5) & (0) & (3) & (0) \end{pmatrix}$	2 0 0 0 (5)(0)(0)(0)	2 0 0 0 (5)(0)(0)(0)	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 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

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### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

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PAGE : 21

0rgan	Findings	Group Name         Control           No. of Animals on Study         38           Grade         1         2         3         4           (%)         (%)         (%)         (%)	$ \begin{array}{c} 750 \text{ ppm} \\ 41 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$ \begin{array}{c} 1500 \text{ ppm} \\ 42 \\ \hline (\%) (\%) (\%) (\%) (\%) (\%) \end{array} $	3000 ppm 39 <u>1 2 3 4</u> (%) (%) (%) (%)
[Digestive s	vstem]				
liver	acidophilic cell focus	<38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<42> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	basophilic cell focus	22 0 0 0 (58) (0) (0) (0)	26 0 0 0 (63) (0) (0) (0)	31 1 0 0 (74) (2) (0) (0)	28 1 0 0 (72) (3) (0) (0)
	vacuolated cell focus	3 0 0 0 (8)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)	0 1 0 0 ( 0) ( 2) ( 0) ( 0)	1 0 0 0 (3)(0)(0)(0)(0)
	mixed cell facus	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 1 0 ( 0) ( 0) ( 2) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	bile duct hyperplasia	25 1 0 0 (66)(3)(0)(0)	30 0 0 0 (73)(0)(0)(0)	34 0 0 0 (81)(0)(0)(0)	14 0 0 0* (36)(0)(0)(0)
Dancreas	atrophy	<pre> &lt;38&gt; 3 2 0 0 ( 8) ( 5) ( 0) ( 0)</pre>	<41> 4 1 0 0 (10) (2) (0) (0)	<42> 3 0 0 0 ( 7) ( 0) ( 0) ( 0)	<39> 2 1 0 0 (5) (3) (0) (0)
[Urinary sys	tem]				
kidney	infarct	<38> 1 0 0 0 (3) (0) (0) (0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<42> 3 0 0 0 (7) (0) (0) (0)	<39> 5 0 0 0 (13) (0) (0) (0)

(c) c:b/a\*100

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

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

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SEX	: FEMALE				PAGE : 22
0rgan	Findings	Group Name         Control           No. of Animals on Study         38           Grade         1         2         3         4           (%)         (%)         (%)         (%)	$ \begin{array}{c} 750 \text{ ppm} \\ 41 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	$ \begin{array}{c} 1500 \text{ ppm} \\ 42 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $	3000 ppm 39 <u>1 2 3 4</u> (%) (%) (%) (%)
[Urinary sy	stem]				
kidney	basophilic change	<38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<42> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<39> 3 0 0 0 (8) (0) (0) (0)
	deposit of hemosiderin	0 1 0 0 ( 0) ( 3) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	deposit of crystal	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)(0)	12 2 0 0 *** (31) (5) (0) (0)
	inflammatory infiltration	1 0 0 0 (3)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	chronic nephropathy	12 20 3 1 (32)(53)(8)(3)	11 26 2 1 (27) (63) (5) (2)	13 20 2 0 (31)(48)(5)(0)	18 9 0 0 *** (46)(23)(0)(0)
	papillary necrosis	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	4 0 0 0 (10) (0) (0) (0)	10 16 0 0 ** (24) (38) (0) (0)	7 28 1 0 ** (18) (72) (3) (0)
	mineralization:cortico-medullary junc	ntion 3 0 0 0 (8)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (3)(0)(0)(0))
	mineralization:papilla	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	5 0 0 0 (12)(0)(0)(0)	13 0 0 0 <b>**</b> (33) (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: 22

Drgan	Findings	Group Name No. of Animals on Study Grade <u>1</u> (%)		rol <u>3 4</u> %) (%)	<u>1</u> (%) (	750 ppm 41 2 3 (%) (%)	$\frac{4}{(\%)}$ $\frac{1}{(\%)}$	1500 42 2 (%)	3	<u>4</u> (%)	<u>1</u> (%)	3000 p 39 2 3 (%) (%	} 4	<u>4</u> %)
Urinary syst	em]													
(idney	mineralization:pelvis	4 (11)	<38> 0 ( 0) (	0 0 0)(0)	0 ( 0) (	<41> 0 0 0) ( 0) (	0 0 0) ( 0)	<42> 0 ( 0) (	0 0) (		1 ( 3) (	<39> 0 ( 0) ( (		0 0)
	urothelial hyperplasia:pelivis	1 ( 3)	0 ( 0) (	0 0 0) ( 0)	0 ( 0) (	0 0 0)(0)(	0 2 0) ( 5)	0 ( 0) (	0 0) (	0 0)	20 (51) (	8 ( 21) ( (	) (	0 *: 0)
	eosinophilic droplet:proximal tubule		2 (5)(	0 0 0)(0)	12 (29) (	2 0 5)(0)(	0 23 0) (55)	2 (5)(	0 0) (	0 * 0)	21 ( 54) (	0 ( 0) ( (		0 * 0)
rin bladd	transitional cell hyperplasia	0 ( 0)	<38> 0 ( 0) (	0 0 0)(0)	0 ( 0) (	<41> 0 0 0) ( 0) (	0 0 0) ( 0)	<42> 0 ( 0) (	0	0 0)	0 ( 0) (			0 0)
Endocrine sy	stem]				·									
ituitary	tubular structure	1 (3)	<38> 0 ( 0) (	0 0 0) ( 0)		<41> 0 0 0) ( 0) (	0 0 0) ( 0)	<41> 0 ( 0) (	0	0 0)	0 ( 0) (			0 0)
	angiectasis	11 ( 29)	0 ( 0) (	0 0 0)(0)	6 (15) (	1 0 2)(0)(	0 11 0) (27)	0 ( 0) (	0 0) (	0 0)	13 (33) (			0 0)

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

(HPT150)

BAIS3

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

PAGE : 23

0rgan	Findings	Group Name Control No. of Animals on Study 38 Grade <u>1 2 3 4</u> (%) (%) (%) (%)	$\begin{array}{c} 750 \text{ ppm} \\ 41 \\ \hline (\%) & (\%) & (\%) & (\%) \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$ \begin{array}{c} 3000 \text{ ppm} \\ 39 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $
[Endocrine sy	stem]				
pituitary	cyst	<38> 13 0 0 0 (34) (0) (0) (0)	<41> 12 0 0 0 (29) (0) (0) (0)	$\begin{array}{c} <41>\\ 14 & 1 & 0 & 0\\ (34) & (2) & (0) & (0) \end{array}$	<39> 9 0 0 0 (23) (0) (0) (0)
	deposit of hemosiderin	3 0 0 0 (8)(0)(0)(0)	2 0 0 0 (5)(0)(0)(0)	5 0 0 0 (12)(0)(0)(0)	3 0 0 0 (8)(0)(0)(0)
	hyperplasia	8 3 0 0 (21)(8)(0)(0)	4 3 0 0 (10) (7) (0) (0)	7 2 0 0 (17) (5) (0) (0)	6 2 0 0 (15) (5) (0) (0)
	Rathke pouch	6 0 0 0 (16) (0) (0) (0)	5 0 0 0 (12) (0) (0) (0)	8 0 0 0 (20)(0)(0)(0)	9 0 0 0 (23)(0)(0)(0)
thyroid	C-cell hyperplasia	<38> 6 2 0 0 (16) (5) (0) (0)	<41> 3 0 0 0 ( 7) ( 0) ( 0) ( 0)	<41> 2 0 0 0 ( 5) ( 0) ( 0) ( 0)	<39> 6 0 0 0 (15) (0) (0) (0)
parathyroid	cyst	<29> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	<30> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<32> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<30> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
adrenal	hemorrhage	<38> 2 0 0 0 ( 5) ( 0) ( 0) ( 0)	<pre> &lt;41&gt;     4 0 0 0     ( 10) ( 0) ( 0) ( 0) </pre>	<42> 3 0 0 0 ( 7) ( 0) ( 0) ( 0)	<39> 6 1 0 0 (15) (3) (0) (0)

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

b: Number of animals with lesion

b

(c) c:b/a \* 100

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

: FEMALE

SEX

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

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PAGE: 24

0rgan	_ Findings	Group Name Control No. of Animals on Study 38 Grade <u>1 2 3 4</u> (%) (%) (%) (%)	$\begin{array}{c} 750 \text{ ppm} \\ 41 \\ \underline{1 \ 2 \ 3 \ 4} \\ \hline (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$	1500 ppm 42 <u>1 2 3 4</u> (%) (%) (%) (%)	3000 ppm 39 <u>1 2 3 4</u> (%) (%) (%) (%)
[Endocrine	system]				
adrenal	peliasis-like lesion	<38> 11 13 1 0 (29) (34) (3) (0)	<41> 21 10 0 0 (51) (24) (0) (0)	<42> 21 6 1 0 (50) (14) (2) (0)	<39> 13 20 0 0 (33) (51) (0) (0)
	cyst	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 2) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)	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)	2 0 0 0 (5)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	hyperplasia:cortical cell	2 0 0 0 (5)(0)(0)(0)	2 0 0 0 (5)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	hyperplasia:medulla	2 0 0 0 (5)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)	0 1 0 0 ( 0) ( 3) ( 0) ( 0)
	focal fatty change:contex	5 0 0 0 (13)(0)(0)(0)	3 0 0 0 (7)(0)(0)(0)	7 0 0 0 (17)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
[Reproducti	ive system]				
DUALTY	cyst	<37> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 2 0 0 0 ( 5) ( 0) ( 0) ( 0)	<42> 4 0 0 0 (10) (0) (0) (0)	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
Grade < a > b	1: Slight 2: Moderate a: Number of animals examined at 1 b: Number of animals with lesion c: b ( a * 100	3: Marked 4: Severe the site			

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

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# SEX : FEMALE

ANIMAL : RAT F344/DuCrj

STUDY NO. : 0267

REPORT TYPE : A1

PAGE: 25

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(HPT150)

(c)

c:b/a\*100

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

Findings\_

0rgan\_

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

Group Name Control 750 ppm 1500 ppm No. of Animals on Study 38 41 42 <u>2 3 4</u> (%) (%) (%) 2 3 2<u>3</u>4 (%)(%)(%) 4 2 3 4 1 (%) (%) (%) (%) (%) (%) (%) (%) (%) (%)

[Reproductive	system]				
uterus	dilatation	<38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<42> 2 0 0 0 ( 5) ( 0) ( 0) ( 0)	<39> 0 1 0 0 ( 0) ( 3) ( 0) ( 0)
	cell debris	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)(0)	0 1 0 0 ( 0) ( 3) ( 0) ( 0)
	cystic endometrial hyperplasia	2 3 0 0 (5)(8)(0)(0)	3 3 1 0 (7)(7)(2)(0)	6 0 0 0 (14)(0)(0)(0)	6 1 1 0 (15)(3)(3)(0)
mammary gl	duct ectasia	<38> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	<41> 0 1 0 0 ( 0) ( 2) ( 0) ( 0)	<42> 3 0 0 0 ( 7) ( 0) ( 0) ( 0)	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	hyperplasia	0 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 0 0 0 (5)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	galactocele	3 1 0 0 (8)(3)(0)(0)	5 0 0 0 (12)(0)(0)(0)	2 0 0 0 (5)(0)(0)(0)	2 0 0 0 (5)(0)(0)(0)
[Special sense	e organs/appandage]				
өуө	cataract	<38> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	<41> 3 0 0 0 ( 7) ( 0) ( 0) ( 0)	<42> 2 0 0 0 ( 5) ( 0) ( 0) ( 0)	<39> 2 0 0 0 (5) (0) (0) (0)

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

Grade

<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

.

PAGE: 26

3000 ppm

3

39

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

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PAGE : 27

0rgan	Findings	Group Name No. of Animals on Study Grade <u>1</u> (%)	Control 38 <u>2 3 4</u> (%) (%) (%)	$ \begin{array}{c} 750 \text{ ppm} \\ 41 \\ \underline{1 \ 2 \ 3 \ 4} \\ \underline{(\%) \ (\%) \ (\%) \ (\%) \ (\%)} \end{array} $	1500 ppm 42 <u>1 2 3 4</u> (%) (%) (%) (%)	$ \begin{array}{c} 3000 \text{ ppm} \\ 39 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $
[Special sens	e organs/appandage]					
еуе	retinal atrophy	5 (13)	<38> 0 1 0 ( 0) ( 3) ( 0)	<41> 0 1 2 0 ( 0) ( 2) ( 5) ( 0)	<42> 3 3 0 0 ( 7) ( 7) ( 0) ( 0)	<39> 4 0 0 0 (10) (0) (0) (0)
	keratitis	1 ( 3)	0 0 0 ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	degeneration:cornea	1 ( 3)	0 0 0 ( 0) ( 0) ( 0)	2 0 0 0 (5)(0)(0)(0)	2 0 0 0 (5)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0
	vascularization:cornea	1 ( 3)	0 0 0 ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
Harder gi	granulation	1 ( 3)	<38> 0 0 0 ( 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<42> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<39> 1 0 0 0 (3) (0) (0) (0)
nasolacr d	inflammation	5 (13)	<38> 0 0 0 ( 0) ( 0) ( 0)	<41> 7 0 0 0 ( 17) ( 0) ( 0) ( 0)	<42> 3 0 0 0 ( 7) ( 0) ( 0) ( 0)	<39> 10 0 0 0 (26) (0) (0) (0)
[Musculoskele	otal system]					
bane	fracture	0 ( 0)	<38> 0 0 0 ( 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<42> 0 1 0 0 ( 0) ( 2) ( 0) ( 0)	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0

(c) c:b/a \* 100

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

)rgan	Findings	Group Name         Control           No. of Animals on Study         38           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%)	$ \begin{array}{c} 750 \text{ ppm} \\ 41 \\ \underline{1 \ 2 \ 3 \ 4} \\ \underline{(\%) \ (\%) \ (\%) \ (\%)} \end{array} $	$ \begin{array}{c} 1500 \text{ ppm} \\ 42 \\ \underline{1  2  3  4} \\ \underline{(\%)  (\%)  (\%)  (\%)} \end{array} $	3000 ppm 39 <u>1 2 3 4</u> (%) (%) (%) (%)
LAUSCU LOSKE ( Done	etal system] osteosclerosis	$\begin{array}{c} <38>\\ 2 & 4 & 1 & 0\\ (5) & (11) & (3) & (0) \end{array}$	<41> 7 3 1 0 (17) (7) (2) (0)	<42> 8 4 1 0 (19) (10) (2) (0)	<39> 4 7 4 0 (10) (18) (10) (0)
-ticulus	ossification	<38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<42> 0 1 0 0 ( 0) ( 2) ( 0) ( 0)	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
Body caviti	es]				
eritoneum	peritonitis	<38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<42> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<39> 0 1 0 0 ( 0) ( 3) ( 0) ( 0)
dipose	granulation	<38> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<42> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)

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(HPT150)

APPENDIX M1

### NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED

RAT : MALE

(2-YEAR STUDY)

#### NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

PAGE : 1

Time-related Weeks	Items	Group Name	Control	750 ppm	1500 ppm	3000 ppm	
0 - 52	NO. OF EXAMINED ANIMALS		0	0	0	0	
	NO. OF ANIMALS WITH TUMORS NO. OF ANIMALS WITH SINGLE TUMORS NO. OF ANIMALS WITH MULTIPLE TUMORS		0 0 0	0 0 0	0 0 0	0 0 0	
	NO. OF BENIGN TUMORS NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS		0 0 0	0 0 0	0 0 0	0 0 0	
53 - 78	NO. OF EXAMINED ANIMALS		1	1	1	0	<u> </u>
	NO. OF ANIMALS WITH TUMORS NO. OF ANIMALS WITH SINGLE TUMORS NO. OF ANIMALS WITH MULTIPLE TUMORS		1 0 1	1 1 0	1 1 0	0 0 0	
	NO. OF BENIGN TUMORS NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS		1 1 2	1 0 1	1 0 1	0 0 0	
79 - 104	NO. OF EXAMINED ANIMALS		10	8	8	4	
	NO. OF ANIMALS WITH TUMORS ', NO. OF ANIMALS WITH SINGLE TUMORS NO. OF ANIMALS WITH MULTIPLE TUMORS		10 1 9	8 3 5	8 1 7	4 1 3	
	NO. OF BENIGN TUMORS NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS		16 7 23	10 4 14	14 6 20	5 2 7	
105 - 105	NO. OF EXAMINED ANIMALS		39	41	41	46	
	NO. OF ANIMALS WITH TUMORS NO. OF ANIMALS WITH SINGLE TUMORS NO. OF ANIMALS WITH MULTIPLE TUMORS		38 17 21	41 17 24	41 22 19	46 19 27	
	NO. OF BENIGN TUMORS NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS		65 6 71	76 6 82	62 8 70	70 9 79	

Time-related Weeks	Items	Group Name	Control	750 ppm	1500 ppm	3000 ppm	
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	50	
	NO. OF ANIMALS WITH TUMORS		49	50	50	50	
	NO. OF ANIMALS WITH SINGLE TUMORS		18	21	24	20	
	NO. OF ANIMALS WITH MULTIPLE TUMORS		31	29	26	30	
	NO. OF BENIGN TUMORS		82	87	77	75	
	NO. OF MALIGNANT TUMORS		14	10	14	11	
	NO. OF TOTAL TUMORS		96	97	91	86	

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### NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj APPENDIX M2

### NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED

RAT : FEMALE

(2-YEAR STUDY)

| me-related<br>Weeks | Items                                                                                                  | Group Name | Control        | 750 ppm        | 1500 ppm      | 3000 ppm      |        |
|---------------------|--------------------------------------------------------------------------------------------------------|------------|----------------|----------------|---------------|---------------|--------|
| 0 - 52              | NO. OF EXAMINED ANIMALS                                                                                |            | 0              | 0              | 0             | 0             |        |
|                     | NO. OF ANIMALS WITH TUMORS<br>NO. OF ANIMALS WITH SINGLE TUMORS<br>NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0<br>0<br>0    | 0<br>0<br>0    | 0<br>0<br>0   | 0<br>0<br>0   |        |
|                     | NO. OF BENIGN TUMORS<br>NO. OF MALIGNANT TUMORS<br>NO. OF TOTAL TUMORS                                 |            | 0<br>0<br>0    | 0<br>0<br>0    | 0<br>0<br>0   | 0<br>0<br>0   |        |
| 53 - 78             | NO. OF EXAMINED ANIMALS                                                                                |            | 0              | 0              | 0             | 3             |        |
|                     | NO. OF ANIMALS WITH TUMORS<br>NO. OF ANIMALS WITH SINGLE TUMORS<br>NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0<br>0<br>0    | 0<br>0<br>0    | 0<br>0<br>0   | 2<br>2<br>0   |        |
|                     | NO. OF BENIGN TUMORS<br>NO. OF MALIGNANT TUMORS<br>NO. OF TOTAL TUMORS                                 |            | 0<br>0<br>0    | 0<br>0<br>0    | 0<br>0<br>0   | 1<br>1<br>2   |        |
| 79 - 104            | NO. OF EXAMINED ANIMALS                                                                                |            | 12             | 9              | 8             | 8             | ······ |
|                     | NO. OF ANIMALS WITH TUMORS<br>NO. OF ANIMALS WITH SINGLE TUMORS<br>NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 12<br>5<br>7   | 9<br>3<br>6    | 8<br>4<br>4   | 7<br>3<br>4   |        |
|                     | NO. OF BENIGN TUMORS<br>NO. OF MALIGNANT TUMORS<br>NO. OF TOTAL TUMORS                                 |            | 10<br>9<br>19  | 11<br>5<br>16  | 11<br>3<br>14 | 9<br>4<br>13  |        |
| 105 - 105           | NO. OF EXAMINED ANIMALS                                                                                |            | 38             | 41             | 42            | 39            |        |
|                     | NO. OF ANIMALS WITH TUMORS<br>NO. OF ANIMALS WITH SINGLE TUMORS<br>NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 26<br>13<br>13 | 32<br>13<br>19 | 25<br>19<br>6 | 27<br>21<br>6 |        |
|                     | NO. OF BENIGN TUMORS<br>NO. OF MALIGNANT TUMORS<br>NO. OF TOTAL TUMORS                                 |            | 38<br>5<br>43  | 45<br>12<br>57 | 29<br>4<br>33 | 32<br>3<br>35 |        |

### NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

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| _                               |                                                                                                                                       |                                                                                                                                       |                                                                                                                                                                                                        |                                                                                                                                           |                                                                                                                                                    |                                                                                                                                                             |
|---------------------------------|---------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|
| is                              | Group Name                                                                                                                            | Control                                                                                                                               | 750 ppm                                                                                                                                                                                                | 1500 ppm .                                                                                                                                | 3000 ppm                                                                                                                                           |                                                                                                                                                             |
| OF EXAMINED ANIMALS             |                                                                                                                                       | 50                                                                                                                                    | 50                                                                                                                                                                                                     | 50                                                                                                                                        | 50                                                                                                                                                 |                                                                                                                                                             |
| OF ANIMALS WITH TUMORS          |                                                                                                                                       | 38                                                                                                                                    | 41                                                                                                                                                                                                     | 33                                                                                                                                        | 36                                                                                                                                                 |                                                                                                                                                             |
|                                 |                                                                                                                                       | 18                                                                                                                                    | 16                                                                                                                                                                                                     | 23                                                                                                                                        | 26                                                                                                                                                 |                                                                                                                                                             |
| OF ANIMALS WITH MULTIPLE TUMORS |                                                                                                                                       | 20                                                                                                                                    | 25                                                                                                                                                                                                     | 10                                                                                                                                        | 10                                                                                                                                                 |                                                                                                                                                             |
| OF BENIGN TUMORS                |                                                                                                                                       | 48                                                                                                                                    | 56                                                                                                                                                                                                     | 40                                                                                                                                        | 12                                                                                                                                                 |                                                                                                                                                             |
| OF MALIGNANT TUMORS             |                                                                                                                                       |                                                                                                                                       |                                                                                                                                                                                                        | 7                                                                                                                                         |                                                                                                                                                    |                                                                                                                                                             |
| OF TOTAL TUMORS                 |                                                                                                                                       | 62                                                                                                                                    | 73                                                                                                                                                                                                     | 47                                                                                                                                        | 50                                                                                                                                                 |                                                                                                                                                             |
|                                 | OF ANIMALS WITH TUMORS<br>OF ANIMALS WITH SINGLE TUMORS<br>OF ANIMALS WITH MULTIPLE TUMORS<br>OF BENIGN TUMORS<br>OF MALIGNANT TUMORS | OF ANIMALS WITH TUMORS<br>OF ANIMALS WITH SINGLE TUMORS<br>OF ANIMALS WITH MULTIPLE TUMORS<br>OF BENIGN TUMORS<br>OF MALIGNANT TUMORS | OF ANIMALS WITH TUMORS       38         OF ANIMALS WITH SINGLE TUMORS       18         OF ANIMALS WITH MULTIPLE TUMORS       20         OF BENIGN TUMORS       48         OF MALIGNANT TUMORS       14 | OF ANIMALS WITH TUMORS3841OF ANIMALS WITH SINGLE TUMORS1816OF ANIMALS WITH MULTIPLE TUMORS2025OF BENIGN TUMORS4856OF MALIGNANT TUMORS1417 | OF ANIMALS WITH TUMORS384133OF ANIMALS WITH SINGLE TUMORS181623OF ANIMALS WITH MULTIPLE TUMORS202510OF BENIGN TUMORS485640OF MALIGNANT TUMORS14177 | OF ANIMALS WITH TUMORS38413336OF ANIMALS WITH SINGLE TUMORS18162326OF ANIMALS WITH MULTIPLE TUMORS20251010OF BENIGN TUMORS48564042OF MALIGNANT TUMORS141778 |

### NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

## APPENDIX N 1

### HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : ALL ANIMALS

(2-YEAR STUDY)

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### HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)

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750 ppm Group Name Control 1500 ppm No. of animals on Study 50 50 50

Findings\_\_\_

| [Integumentary | system/appandage]              |                 |                  |                 |                 |
|----------------|--------------------------------|-----------------|------------------|-----------------|-----------------|
| skin/app       | squamous cell papilloma        | <50><br>0 ( 0%) | <50><br>1 ( 2%)  | <50><br>1 ( 2%) | <50><br>1 ( 2%) |
|                | trichcepithelioma              | 0 ( 0%)         | 1 ( 2%)          | 0 ( 0%)         | 0 ( 0%)         |
|                | basal cell epithelioma         | 0 ( 0%)         | 1 ( 2%)          | 0 ( 0%)         | 0 ( 0%)         |
|                | keratoacanthoma                | 0 ( 0%)         | 3 ( 6%)          | 0 ( 0%)         | 0 ( 0%)         |
|                | sebaceous adenoma              | 0 ( 0%)         | 1 ( 2%)          | 0 ( 0%)         | 1 ( 2%)         |
| subcutis       | fibroma                        | <50><br>2 ( 4%) | <50><br>6 ( 12%) | <50><br>4 ( 8%) | <50><br>1 ( 2%) |
|                | Lipoma                         | 0 ( 0%)         | 0 ( 0%)          | 0 ( 0%) .       | 1 ( 2%)         |
|                | xanthoma                       | 0 ( 0%)         | 0 ( 0%)          | 2 ( 4%)         | 0 ( 0%)         |
|                | liposarcoma                    | 0 ( 0%)         | 0 ( 0%)          | 1 ( 2%)         | 0 ( 0%)         |
|                | rhabdomyosarcoma               | 0 ( 0%)         | 1 ( 2%)          | 0 ( 0%)         | 0 ( 0%)         |
|                | schwannoma:malignant           | 0 ( 0%)         | 0 ( 0%)          | 1 ( 2%)         | 0 ( 0%)         |
|                | malignant fibrous histiocytoma | 1 ( 2%)         | 0 ( 0%)          | 0 ( 0%)         | 0 ( 0%)         |
|                | sarcoma:NOS                    | 1 ( 2%)         | 0 ( 0%)          | 0 ( 0%)         | 1 ( 2%)         |

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

b (c) b : Number of animals with neoplasm c:b/a\*100

(HPT085)

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PAGE : 1

3000 ppm

50

| STUDY NO. : 0267<br>ANIMAL : RAT F344/DuCrj<br>REPORT TYPE : A1 |                              | HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)<br>ALL ANIMALS (0-105W) |                 |                 |                 |                 |      |  |
|-----------------------------------------------------------------|------------------------------|------------------------------------------------------------------------------|-----------------|-----------------|-----------------|-----------------|------|--|
|                                                                 | MALE                         |                                                                              |                 |                 |                 | PAG             | E: 2 |  |
| Organ                                                           | Findings                     | Group Name<br>No. of animals on Study                                        | Control<br>50   | 750 ppm<br>50   | 1500 ppm<br>50  | 3000 ppm<br>50  |      |  |
| [Respiratory                                                    | system]                      |                                                                              |                 |                 |                 |                 |      |  |
| lung                                                            | bronchiolar-alveolar adenoma |                                                                              | <50><br>3 ( 6%) | <50><br>2 ( 4%) | <50><br>2 ( 4%) | <50><br>1 ( 2%) |      |  |
|                                                                 | bronchial carcinoma          |                                                                              | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)         | 1 (2%)          |      |  |
| [Hematopoieti                                                   | c system]                    |                                                                              |                 |                 |                 |                 |      |  |
| spleen                                                          | histiocytic sarcoma          |                                                                              | <50><br>0 ( 0%) | <49><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) |      |  |
|                                                                 | mononuclear cell leukemia    |                                                                              | 4 ( 8%)         | 1 ( 2%)         | 3 ( 6%)         | 3 ( 6%)         |      |  |
| [Circulatory                                                    | system]                      |                                                                              |                 |                 |                 |                 |      |  |
| hear-t                                                          | schwannoma:malignant         |                                                                              | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |      |  |
| [Digestive sy                                                   | vstem]                       |                                                                              |                 |                 |                 |                 |      |  |
| oral cavity                                                     | squameus cell papilloma      |                                                                              | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) |      |  |
|                                                                 | basal cell carcinoma         |                                                                              | 1 ( 2%)         | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)         |      |  |
| salivary gl                                                     | adenocarcinoma               |                                                                              | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) |      |  |
| stomach                                                         | squamous cell carcinoma      |                                                                              | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) |      |  |
| large intes                                                     | adenoma                      |                                                                              | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) |      |  |

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

b (c) b: Number of animals with neoplasm c: b/a \* 100

(HPT085)

|                | 0267<br>RAT F344/DuCrj<br>A1 | HISTOLOGICAL FINDINGS : NEOF<br>ALL ANIMALS (0-105W) | PLASTIC LESIONS (S | UMMARY)          |                   |                  |     |
|----------------|------------------------------|------------------------------------------------------|--------------------|------------------|-------------------|------------------|-----|
|                | NALE                         |                                                      |                    |                  |                   | PAGE             | : 3 |
| 0rgan          | Findings                     | Group Name<br>No. of animals on Study                | Control<br>50      | 750 ppm<br>50    | 1500 maa<br>50    | 3000 ppm<br>50   |     |
| [Digestive sys | stem]                        |                                                      |                    |                  |                   |                  |     |
| Liver          | hepatocellular adenoma       |                                                      | <50><br>0 ( 0%)    | <50><br>1 ( 2%)  | <50><br>1 ( 2%)   | <50><br>1 ( 2%)  |     |
| (Urinary syste | em]                          |                                                      |                    |                  |                   |                  |     |
| kidney         | transitional cell carcinoma  |                                                      | <50><br>0 ( 0%)    | <50><br>1 ( 2%)  | <50><br>0 ( 0%)   | <50><br>0 ( 0%)  |     |
| [Endocrine sy  | stem]                        |                                                      |                    |                  |                   |                  |     |
| pituitary      | adenoma                      |                                                      | <50><br>17 ( 34%)  | <50><br>14 (28%) | <50><br>12 ( 24%) | <50><br>5 ( 10%) |     |
|                | adenocarcinoma               |                                                      | 2 ( 4%)            | 1 ( 2%)          | 0 ( 0%)           | 0 ( 0%)          |     |
| thyroid        | C-cell adenoma               |                                                      | <50><br>3 ( 6%)    | <50><br>6 ( 12%) | <50><br>1 ( 2%)   | <50><br>10 (20%) |     |
|                | follicular adenoma           |                                                      | 1 ( 2%)            | 0 ( 0%)          | 0 ( 0%)           | 0 ( 0%)          |     |
|                | follicular adenocarcinoma    |                                                      | 1 ( 2%)            | 0 ( 0%)          | 0 ( 0%)           | 0 ( 0%)          |     |
| parathyroid    | adenoma                      |                                                      | <40><br>0 ( 0%)    | <42><br>0 ( 0%)  | <43><br>1 ( 2%)   | <41><br>0 ( 0%)  |     |
| panc islet     | islet cell adenoma           |                                                      | <50><br>3 ( 6%)    | <50><br>5 ( 10%) | <50><br>3 ( 6%)   | <50><br>0 ( 0%)  |     |
|                | islet cell adenocarcinoma    |                                                      | 0 ( 0%)            | 0 ( 0%)          | 0 ( 0%)           | 1 ( 2%)          |     |
| adrenal        | pheachromocytoma             |                                                      | <50><br>3 ( 6%)    | <50><br>6 ( 12%) | <50><br>1 ( 2%)   | <50><br>3 ( 6%)  |     |

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c:b/a\*100

b (c) (HPT085)

<a>

a : Number of animals examined at the site

b: Number of animals with neoplasm

| REPORT TYPE :  | RAT F344/DuC-j<br>A1<br>MALE | ALL ANIMALS (0-105W)                  |    |                |    |                |    |               |    |               | PAGE: 4 |
|----------------|------------------------------|---------------------------------------|----|----------------|----|----------------|----|---------------|----|---------------|---------|
| 0rgan          | Findings                     | Group Name<br>No. of animals on Study |    | Control<br>50  |    | 750 ppm<br>50  | ]  | 500 ppm<br>50 | 3  | 000 ppm<br>50 |         |
| [Endocrine sys | rtem]                        |                                       |    |                |    |                |    |               |    |               |         |
| adrenal.       | pheochromocytoma:malignant   |                                       | 2  | <50><br>( 4%)  | 3  | <50><br>( 6%)  | 2  | <50><br>( 4%) | 1  | <50><br>( 2%) |         |
| [Reproductive  | system]                      |                                       |    |                |    |                |    |               |    |               |         |
| testis         | interstitial cell tumor      |                                       | 46 | <50><br>( 92%) | 39 | <50><br>( 78%) | 48 | <50><br>(96%) | 48 | <50><br>(96%) |         |
| mammary gl     | fibroadenoma                 |                                       | 2  | <50><br>( 4%)  | 1  | <50><br>( 2%)  | 1  | <50><br>( 2%) | 0  | <50><br>( 0%) |         |
|                | adenocarcinoma               |                                       | 0  | ( 0%)          | 0  | ( 0%)          | 1  | ( 2%)         | 0  | ( 0%)         |         |
| prep/cli gl    | adenoma                      |                                       | 2  | <50><br>( 4%)  | 0  | <50><br>( 0%)  | 0  | <50><br>( 0%) | 1  | <50><br>( 2%) |         |
| (Nervous syste | m]                           |                                       |    |                |    |                |    |               |    |               |         |
| brain          | malignant reticulosis        |                                       | 0  | <50><br>( 0%)  | 0  | <50><br>( 0%)  | 1  | <50><br>( 2%) | 0  | <50><br>( 0%) |         |
| spinal cord    | malignant reticulosis        |                                       | 0  | <50><br>( 0%)  | 0  | <50><br>( 0%)  | 1  | <50><br>( 2%) | 0  | <50><br>( 0%) |         |
| [Special sense | argans/appandage]            |                                       |    |                |    |                |    |               |    |               |         |
| Zymbal gl      | squamous cell carcinoma      |                                       | 0  | <50><br>( 0%)  | 1  | <50><br>( 2%)  | 1  | <50><br>( 2%) | 0  | <50><br>( 0%) |         |
| [Musculaskelet | al system]                   |                                       |    |                |    |                |    |               |    |               |         |
| vertebra       | chordoma:malignant           |                                       | 0  | <50><br>( 0%)  | 1  | <50><br>( 2%)  | 0  | <50><br>( 0%) | 0  | <50><br>( 0%) |         |

(a) a : Number of animals examined at the site

b (c) c:b/a\*100 b : Number of animals with neoplasm

STUDY NO. : 0267

ANIMAL : RAT F344/DuCrj

# HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)

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| REPORT TYPE :                     | RAT F344/DUG-J<br>A1<br>MALE               | ALL ANIMALS (0-1050)                  |                 |                 |                 | PAGE            |
|-----------------------------------|--------------------------------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Organ                             | Findings                                   | Group Name<br>No. of animals on Study | Control<br>50   | 750 ppm<br>50   | 1500 ppm<br>50  | 3000 ppm<br>50  |
| [Body cavities                    | sl                                         |                                       |                 |                 |                 |                 |
| pleura                            | mesothelioma                               |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) |
| peritoneum                        | mesothelioma                               |                                       | <50><br>1 ( 2%) | <50><br>1 ( 2%) | <50><br>2 ( 4%) | <50><br>1 ( 2%) |
| <pre> &lt; a &gt;     b (c)</pre> | a : Number of animals examined at the site | / a * 100                             | 1 ( 2%)         | 1 ( 2%)         | 2 ( 4%)         | 1 ( 2%)         |

(HPT085)

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### HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj

# APPENDIX N 2

### HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : ALL ANIMALS

(2-YEAR STUDY)

### HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)

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PAGE: 6

| -gan         |                                | p Name<br>of animals on Study | Control<br>50  | 750 ppm<br>50   | 1500 ppm<br>50   | 3000 ppm<br>50  |
|--------------|--------------------------------|-------------------------------|----------------|-----------------|------------------|-----------------|
| Integumentar | y system/appandage]            |                               |                |                 |                  |                 |
| (in/app      | squamous cell papilloma        | 0                             | <50><br>( 0%)  | <50><br>1 ( 2%) | <50><br>0 ( 0%)  | <50><br>0 ( 0%) |
|              | squamous cell carcinoma        | 0                             | ( 0%)          | 0 ( 0%)         | 1 ( 2%)          | 0 ( 0%)         |
|              | sebaceous adenocarcinoma       | 1                             | ( 2%)          | 0 ( 0%)         | 0 ( 0%)          | 0 ( 0%)         |
| bcutis       | fibroma                        | . 1                           | <50><br>( 2%)  | <50><br>0 ( 0%) | <50><br>0 ( 0%)  | <50><br>0 ( 0%) |
|              | schwannoma:malignant           | 0                             | ( 0%)          | 0 ( 0%)         | 0 ( 0%)          | 1 ( 2%)         |
|              | malignant fibrous histiocytoma | 0                             | ( 0%)          | 0 ( 0%)         | 0 ( 0%)          | 1 ( 2%)         |
| Respiratory  | system]                        |                               |                |                 |                  |                 |
| asal cavit   | adenoma                        | 1                             | <50><br>( 2%)  | <50><br>0 ( 0%) | <50><br>0 ( 0%)  | <50><br>0 ( 0%) |
| lematopoieti | c system]                      |                               |                |                 |                  |                 |
| leen         | mononuclear cell leukemia      | 6                             | <50><br>( 12%) | <50><br>4 ( 8%) | <50><br>5 ( 10%) | <50><br>3 ( 6%) |
| )igestive sy | rstem]                         |                               |                |                 |                  |                 |
| tomach       | squamous cell carcinoma        | 0                             | <50><br>( 0%)  | <50><br>0 ( 0%) | <50><br>0 ( 0%)  | <50><br>1 ( 2%) |
| all intes    | leiomyoma                      | 0                             | <50><br>( 0%)  | <50><br>1 ( 2%) | <50><br>0 ( 0%)  | <50><br>1 ( 2%) |

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

b (c) b: Number of animals with neoplasm c: b/a \* 100

(HPT085)

|               | : 0267<br>: RAT F344/DuCrj<br>: A1 | HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)<br>ALL ANIMALS (0-105W) |                   |                   |                  |                  |       |  |
|---------------|------------------------------------|------------------------------------------------------------------------------|-------------------|-------------------|------------------|------------------|-------|--|
|               | FEMALE                             |                                                                              |                   |                   |                  | PA               | GE: 7 |  |
| 0rgan         | Findings                           | Group Name<br>No. of animals on Study                                        | Control<br>50     | 750 ppm<br>50     | 1500 ppm<br>50   | 3000 ppm<br>50   |       |  |
| [Endocrine sy | vstem]                             |                                                                              |                   |                   |                  |                  |       |  |
| pituitary     | adenoma                            |                                                                              | <50><br>16 ( 32%) | <50><br>23 ( 46%) | <49><br>17 (35%) | <50><br>12 (24%) |       |  |
|               | adenocarcinoma                     |                                                                              | 1 ( 2%)           | 0 ( 0%)           | 0 ( 0%)          | 0 ( 0%)          |       |  |
| thyroid       | C-cell adenoma                     |                                                                              | <49><br>5 ( 10%)  | <50><br>5 ( 10%)  | <49><br>5 ( 10%) | <50><br>6 ( 12%) |       |  |
|               | C-cell carcinoma                   |                                                                              | 0 ( 0%)           | 2 ( 4%)           | 0 ( 0%)          | 1 ( 2%)          |       |  |
|               | follicular adenocarcinoma          |                                                                              | 0 ( 0%)           | 1 ( 2%)           | 0 ( 0%)          | 0 ( 0%)          |       |  |
| panc islet    | islet cell adenoma                 |                                                                              | <50><br>1 ( 2%)   | <50><br>0 ( 0%)   | <50><br>0 ( 0%)  | <50><br>0 ( 0%)  |       |  |
| adrenal       | pheochromocytoma                   |                                                                              | <50><br>4 ( 8%)   | <50><br>2 ( 4%)   | <50><br>1 ( 2%)  | <50><br>0 ( 0%)  |       |  |
|               | pheochromocytoma:malignant         |                                                                              | 1 ( 2%)           | 0 ( 0%)           | 0 ( 0%)          | 0 ( 0%)          |       |  |
| [Reproductive | e system]                          |                                                                              |                   |                   |                  |                  |       |  |
| uterus        | adenoma                            |                                                                              | <50><br>0 ( 0%)   | <50><br>0 ( 0%)   | <50><br>1 ( 2%)  | <50><br>0 ( 0%)  |       |  |
|               | Le i omyoma                        |                                                                              | 1 (2%)            | 0 ( 0%)           | 0 ( 0%)          | 1 ( 2%)          |       |  |
|               | endometrial stromal polyp          |                                                                              | 8 (16%)           | 12 (24%)          | 9 (18%)          | 15 ( 30%)        |       |  |
|               | endometrial stromal sarcoma        |                                                                              | 1 (2%)            | 4 ( 8%)           | 0 ( 0%)          | 0 ( 0%)          |       |  |
|               |                                    |                                                                              |                   |                   |                  |                  |       |  |

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<a>> a : Number of animals examined at the site c:b/a\*100

b (c) b : Number of animals with neoplasm

(HPT085)

| STUDY NO. : 0267<br>ANIMAL : RAT F344/DLC-j<br>REPORT TYPE : A1<br>SEX : FEMALE |                         | HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)<br>ALL ANIMALS (0-105W) |                 |                 |                 |                 |     |  |  |
|---------------------------------------------------------------------------------|-------------------------|------------------------------------------------------------------------------|-----------------|-----------------|-----------------|-----------------|-----|--|--|
| SEX :                                                                           | FEMALE                  |                                                                              | ·····           |                 |                 | PAGE            | : 8 |  |  |
| 0rgan                                                                           | Findings                | Group Name<br>No. of animals on Study                                        | Control<br>50   | 750 ppm<br>50   | 1500 ppm<br>50  | 3000 ppm<br>50  |     |  |  |
| [Reproductive                                                                   | system]                 |                                                                              |                 |                 |                 |                 |     |  |  |
| mammary gl                                                                      | adenoma                 |                                                                              | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) |     |  |  |
|                                                                                 | fibroadenoma            |                                                                              | 8 (16%)         | 7 (14%)         | 5 (10%)         | 6 (12%)         |     |  |  |
|                                                                                 | adenocarcinoma          |                                                                              | 3 (6%)          | 4 ( 8%)         | 0 ( 0%)         | 0 ( 0%)         |     |  |  |
| prep/cli gl                                                                     | adenoma                 |                                                                              | <50><br>2 ( 4%) | <50><br>4 ( 8%) | <50><br>2 ( 4%) | <50><br>1 ( 2%) |     |  |  |
|                                                                                 | keratoacanthoma         |                                                                              | 0 ( 0%)         | 1 ( 2%)         | 0 ( 0%)         | 0 ( 0%)         |     |  |  |
| (Nervous syste                                                                  | [me                     |                                                                              |                 |                 |                 |                 |     |  |  |
| brain                                                                           | malignant reticulosis   |                                                                              | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <49><br>0 ( 0%) |     |  |  |
| [Special sense                                                                  | e organs/appandage]     |                                                                              |                 |                 |                 |                 |     |  |  |
| Zymbal gi                                                                       | squamous cell papilloma |                                                                              | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |     |  |  |
|                                                                                 | adenocarcinoma          |                                                                              | 0 ( 0%)         | 1 ( 2%)         | 0 ( 0%)         | 0 ( 0%)         |     |  |  |
| [Body cavities                                                                  | 5]                      |                                                                              |                 |                 |                 |                 |     |  |  |
| peritoneum                                                                      | leiomyosarcoma          |                                                                              | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |     |  |  |

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

b (c) b : Number of animals with neoplasm c:b/a\*100

(HPT085)

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# APPENDIX O 1

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

RAT : MALE

(2-YEAR STUDY)

#### STUDY No. : 0267 ANIMAL : RAT F344/DuCrj SEX : MALE

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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PAGE: 1

| Group Name                                            | Control                           | 750 ppm            | 1500 ppm           | 3000 ppm           |  |
|-------------------------------------------------------|-----------------------------------|--------------------|--------------------|--------------------|--|
|                                                       | SITE : skin/appendage             |                    |                    |                    |  |
| umor rate                                             | TUMOR : keratoacanthoma           |                    |                    |                    |  |
| Overall rates(a)                                      | 0/50( 0.0)                        | 3/50( 6.0)         | 0/50( 0.0)         | 0/50( 0.0)         |  |
| djusted rates(b)                                      | 0.0                               | 7.32               | 0.0                | 0.0                |  |
| Terminal rates(c)<br>tatistical analysis<br>Peto test | 0/39( 0.0)                        | 3/41(7.3)          | 0/41( 0.0)         | 0/46( 0.0)         |  |
| Standard method(d)                                    | P =                               |                    |                    |                    |  |
| Prevalence method(d)                                  | P = 0.8220                        |                    |                    |                    |  |
| Combined analysis(d)                                  | P =                               |                    |                    |                    |  |
| Cochran-Armitage test(e)<br>Fisher Exact test(e)      | P = 0.3762                        | D 0 1005           | D 0 5000           |                    |  |
| FISHER EXACT TEST(E)                                  |                                   | P = 0.1325         | P = 0.5000         | P = 0.5000         |  |
|                                                       | SITE : subcutis                   |                    |                    |                    |  |
| umor rate                                             | TUMOR : fibroma                   |                    |                    |                    |  |
| Overali rates(a)                                      | 2/50( 4.0)                        | 6/50(12,0)         | 4/50( 8.0)         | 1/50( 2.0)         |  |
| Adjusted rates(b)                                     | 5.13                              | 14.63              | 4,55               | 2.17               |  |
| Terminal rates(c)                                     | 2/39( 5.1)                        | 6/41(14.6)         | 1/41(2.4)          | 1/46( 2.2)         |  |
| tatistical analysis                                   |                                   |                    |                    |                    |  |
| Peto test<br>Standard method(d)                       | P = 0.3989                        |                    |                    |                    |  |
| Prevalence method(d)                                  | P = 0.8782                        |                    |                    |                    |  |
| Combined analysis(d)                                  | P = 0.8347                        |                    |                    |                    |  |
| Cochran-Armitage test(e)                              | P = 0.3570                        |                    |                    |                    |  |
| Fisher Exact test(e)                                  |                                   | P = 0.1606         | P = 0.3574         | P = 0.4926         |  |
|                                                       | SITE : lung                       |                    |                    |                    |  |
|                                                       | TUMOR : bronchiolar-alveolar ader | ioma               |                    |                    |  |
| 'umor rate<br>Oursell meter(-)                        |                                   |                    |                    |                    |  |
| Overall rates(a)<br>Adjusted rates(b)                 | 3/50( 6.0)<br>6.98                | 2/50( 4.0)<br>4.88 | 2/50( 4.0)         | 1/50( 2.0)         |  |
| Terminal rates(c)                                     | 2/39(5.1)                         | 4.88<br>2/41( 4.9) | 4.88<br>2/41( 4.9) | 2.17<br>1/46( 2.2) |  |
| tatistical analysis                                   | _,                                |                    | 4/31( 3.0)         | 1/40( 4.4)         |  |
| Peto test                                             | _                                 |                    |                    |                    |  |
| Standard method(d)                                    | P =                               |                    |                    |                    |  |
| Prevalence method(d)<br>Combined analysis(d)          | P = 0.8469<br>P =                 |                    |                    |                    |  |
| Cochran-Armitage test(e)                              | P = 0.3291                        |                    |                    |                    |  |
| Fisher Exact test(e)                                  |                                   | P = 0.4909         | P = 0.4909         | P = 0.3235         |  |

| Group Name                                       | Control                           | 750 ppm      | 1500 ppm     | 3000 ppm    |  |
|--------------------------------------------------|-----------------------------------|--------------|--------------|-------------|--|
|                                                  | SITE : spleen                     |              |              |             |  |
| fumor rate                                       | TUMOR : mononuclear cell leukemia |              |              |             |  |
| Overall rates(a)                                 | 4/50( 8.0)                        | 1/49( 2.0)   | 3/50( 6.0)   | 3/50( 6.0)  |  |
| Adjusted rates(b)                                | 2.56                              | 2.44         | 4.88         | 6,52        |  |
| Terminal rates(c)                                | 1/39( 2.6)                        | 1/41( 2.4)   | 2/41( 4.9)   | 3/46( 6.5)  |  |
| Statistical analysis                             |                                   |              | ,,           | 0,10( 010)  |  |
| Peto test                                        |                                   |              |              |             |  |
| Standard method(d)                               | P = 0.9666                        |              |              |             |  |
| Prevalence method(d)                             | P = 0.1494                        |              |              |             |  |
| Combined analysis(d)<br>Cochran-Armitage test(e) | P = 0.5740<br>P = 0.9513          |              |              |             |  |
| Fisher Exact test(e)                             | F = 0.9515                        | P = 0.2063   | P = 0.4895   | P = 0.4895  |  |
|                                                  |                                   | 1 - 0.2003   | r - 0.4095   | P = 0.4895  |  |
|                                                  | SITE : pituitary gland            |              |              |             |  |
|                                                  | TUMOR : adenoma                   |              |              |             |  |
| lumor rate                                       |                                   |              |              |             |  |
| Overall rates(a)                                 | 17/50(34.0)                       | 14/50(28.0)  | 12/50(24.0)  | 5/50( 10.0) |  |
| Adjusted rates(b)                                | 34.15                             | 19.51        | 24.39        | 10.64       |  |
| Terminal rates(c)                                | 13/39( 33.3)                      | 8/41(19.5)   | 10/41(24.4)  | 4/46(8.7)   |  |
| Statistical analysis                             |                                   |              |              |             |  |
| Peto test                                        | D 0.0505                          |              |              |             |  |
| Standard method(d)                               | P = 0.9537                        |              |              |             |  |
| Preualence method(d)<br>Combined analysis(d)     | P = 0.9930<br>P = 0.9986          |              |              |             |  |
| Cochran-Armitage test(e)                         | P = 0.0036**                      |              |              |             |  |
| Fisher Exact test(e)                             | 1 - 0.0000++                      | P = 0.3959   | P = 0.2725   | P = 0.0166* |  |
|                                                  |                                   | 1 - 0,000    | r - 0.2725   | P = 0.0100* |  |
|                                                  | SITE : pituitary gland            |              |              |             |  |
|                                                  | TUMOR : adenoma, adenocarcinoma   |              |              |             |  |
| Tumor rate                                       |                                   |              |              |             |  |
| Overall rates(a)                                 | 19/50( 38.0)                      | 15/50( 30.0) | 12/50(24.0)  | 5/50( 10.0) |  |
| Adjusted rates(b)                                | 36.59                             | 19.51        | 24.39        | 10.64       |  |
| Terminal rates(c)                                | 14/39( 35.9)                      | 8/41( 19.5)  | 10/41( 24.4) | 4/46( 8.7)  |  |
| Statistical analysis                             |                                   |              |              |             |  |
| Peto test                                        | D = 0.0019                        |              |              |             |  |
| Standard method(d)<br>Prevalence method(d)       | P = 0.9813<br>P = 0.9965          |              |              |             |  |
|                                                  |                                   |              |              |             |  |
| Combined analysis(d)                             | P = 0.99997                       |              |              |             |  |
| Combined analysis(d)<br>Cochran-Armitage test(e) | P = 0.9997<br>P = 0.0009**        |              |              |             |  |

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STUDY No. : 0267 ANIMAL : RAT F344/DuCrj SEX : MALE

SEX

PAGE: 2

| EX : MALE                                                          |                                                        |                         |            |                   | PAGE : |
|--------------------------------------------------------------------|--------------------------------------------------------|-------------------------|------------|-------------------|--------|
| Group Name                                                         | Control                                                | 750 ppm                 | 1500 ppm   | 3000 ppm          |        |
|                                                                    | SITE : thyroid                                         |                         |            |                   |        |
| Tumor rate                                                         | TUMOR : C-cell adenoma                                 |                         |            |                   |        |
| Overall rates(a)                                                   | 3/50( 6.0)                                             | 6/50(12.0)              | 1/50( 2.0) | 10/50( 20.0)      |        |
| Adjusted rates(b)                                                  | 7.69                                                   | 14.63                   | 2.44       | 21,74             |        |
| Terminal rates(c)<br>tatistical analysis<br>Peto test              | 3/39( 7.7)                                             | 6/41(14.6)              | 1/41( 2.4) | 10/46(21.7)       |        |
| Standard method(d)                                                 | P =                                                    |                         |            |                   |        |
| Prevalence method(d)                                               | P = 0.0396*                                            |                         |            |                   |        |
| Combined analysis(d)                                               | P =                                                    |                         |            |                   |        |
| Cochran-Armitage test(e)                                           | P = 0.0383*                                            |                         |            |                   |        |
| Fisher Exact test(e)                                               |                                                        | P = 0.2728              | P = 0.3235 | P = 0.0604        |        |
| Tumor rate                                                         | SITE : pancreas islet<br>TUMOR : islet cell adenoma    |                         |            |                   |        |
| Overall rates(a)                                                   | 3/50( 6.0)                                             | 5/50( 10.0)             | 3/50( 6.0) | 0/50( 0.0)        |        |
| Adjusted rates(b)                                                  | 6.67                                                   | 12.20                   | 7.32       | 0.0               |        |
| Terminal rates(c)<br>Statistical analysis                          | 1/39( 2.6)                                             | 5/41(12.2)              | 3/41(7.3)  | 0/46( 0.0)        |        |
| Peto test<br>Standard method(d)                                    | P =                                                    |                         |            | ,                 |        |
| Prevalence method(d)                                               | P = 0.9658                                             |                         |            |                   |        |
| Combined analysis(d)                                               | P =                                                    |                         |            |                   |        |
| Cochran-Armitage test(e)                                           | P = 0.0836                                             |                         |            |                   |        |
| Fisher Exact test(e)                                               |                                                        | P = 0.3790              | P = 0.3392 | P = 0.1325        |        |
|                                                                    | SITE : pancreas islet<br>TUMOR : islet cell adenoma,is | let cell adenocarcinoma |            |                   |        |
| Tumor rate<br>Overall rates(a)                                     | 3/50( 6.0)                                             | 5/50( 10.0)             | 3/50( 6.0) | 1/50( 0.0)        |        |
| Adjusted rates(b)                                                  | 6.67                                                   | 12,20                   | 7,32       | 1/50( 2.0)<br>0.0 |        |
| Terminal rates(c)<br>Statistical analysis<br>Peto test             | 1/39( 2.6)                                             | 5/41(12.2)              | 3/41(7.3)  | 0/46( 0.0)        |        |
| Standard method(d)<br>Prevalence method(d)<br>Combined analysis(d) | P = 0.1080<br>P = 0.9658<br>P = 0.8932                 |                         |            |                   |        |
| Cochran-Armitage test(e)                                           | P = 0.2271                                             | D = 0.0700              | D 0. 0000  | D 0 0007          |        |
| Fisher Exact test(e)                                               |                                                        | P = 0.3790              | P = 0.3392 | P = 0.3235        |        |

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STUDY No. : 0267

|                                                       |                                                  |                     |                    |                                            | AGE: 4                                        |
|-------------------------------------------------------|--------------------------------------------------|---------------------|--------------------|--------------------------------------------|-----------------------------------------------|
| Group Name                                            | Control                                          | 750 ppm             | 1500 ppm           | 3000 ppm                                   |                                               |
|                                                       | SITE : adrenal gland<br>TUMOR : pheochromocytoma |                     |                    |                                            | <u>, , , , , , , , , , , , , , , , , , , </u> |
| Tumor rate                                            |                                                  |                     |                    |                                            |                                               |
| Overall rates(a)                                      | 3/50( 6.0)                                       | 6/50(12.0)          | 1/50( 2.0)         | 3/50( 6.0)                                 |                                               |
| Adjusted rates(b)                                     | 7.69                                             | 14.63               | 2.44               | 4.35                                       |                                               |
| Terminal rates(c)<br>Hatistical analysis<br>Peto test | 3/39( 7.7)                                       | 6/41( 14.6)         | 1/41( 2.4)         | 2/46( 4.3)                                 |                                               |
| Standard method(d)                                    | P = 0.1175                                       |                     |                    |                                            |                                               |
| Prevalence method(d)                                  | P = 0.8857                                       |                     |                    |                                            |                                               |
| Combined analysis(d)                                  | P = 0.7640                                       |                     |                    |                                            |                                               |
| Cochran-Armitage test(e)<br>Fisher Exact test(e)      | P = 0.5938                                       | D = 0.0799          | D A 9995           | D 0.0000                                   |                                               |
|                                                       |                                                  | P = 0.2728          | P = 0.3235         | P = 0.3392                                 |                                               |
|                                                       | SITE : adrenal gland                             |                     |                    |                                            |                                               |
| lumor rate                                            | TUMOR : pheochromocytoma:maligne                 | ant                 |                    |                                            |                                               |
| Overall rates(a)                                      | 2/50( 4.0)                                       | 3/50( 6.0)          | 2/50( 4.0)         | 1/50( 2.0)                                 |                                               |
| Adjusted rates(b)                                     | 2,56                                             | 4.88                | 4,44               | 2.17                                       |                                               |
| Terminal rates(c)                                     | 1/39( 2.6)                                       | 2/41( 4.9)          | 1/41( 2.4)         | 1/46( 2.2)                                 |                                               |
| tatistical analysis                                   |                                                  |                     |                    |                                            |                                               |
| Peto test                                             | D 0 0001                                         |                     |                    |                                            |                                               |
| Standard method(d)<br>Prevalence method(d)            | P = 0.8831<br>P = 0.5675                         |                     |                    |                                            |                                               |
| Combined analysis(d)                                  | P = 0.3375<br>P = 0.7778                         |                     |                    |                                            |                                               |
| Cochran-Armitage test(e)                              | P = 0.4642                                       |                     |                    |                                            |                                               |
| Fisher Exact test(e)                                  |                                                  | P = 0.4909          | P = 0.3088         | P = 0.4926                                 |                                               |
|                                                       | SITE : adrenal gland                             | ······              |                    | nan ng |                                               |
| m .                                                   | TUMOR : pheachromocytoma, pheach                 | omocytoma:malignant |                    |                                            |                                               |
| Tumor rate<br>Overall rates(a)                        | 5/50(10.0)                                       | 9/50(18.0)          | 2/50/ 6 0)         |                                            |                                               |
| Adjusted rates(b)                                     | 10.26                                            | 9/50(18.0)<br>19.51 | 3/50( 6.0)<br>6.67 | 4/50( 8.0)<br>6.52                         |                                               |
| Terminal rates(c)                                     | 4/39( 10.3)                                      | 8/41(19.5)          | 2/41( 4.9)         | 3/46( 6.5)                                 |                                               |
| Statistical analysis                                  |                                                  |                     |                    | , (                                        |                                               |
| Peto test                                             | D 0 7001                                         |                     |                    |                                            |                                               |
| Standard method(d)<br>Prevalence method(d)            | P = 0.5321<br>P = 0.8488                         |                     |                    |                                            |                                               |
| Combined analysis(d)                                  | P = 0.8488<br>P = 0.8413                         |                     |                    |                                            |                                               |
| Cochran-Armitage test(e)                              | P = 0.3699                                       |                     |                    |                                            |                                               |
| Fisher Exact test(e)                                  |                                                  | P = 0.2379          | P = 0.3790         | P = 0.4883                                 |                                               |
|                                                       |                                                  |                     |                    |                                            |                                               |

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STUDY No. : 0267 ANIMAL : RAT F344/DuCrj SEX : MALE

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| SEX : MALE                                                                                      |                                              |                                     |                                     |                                     | PAGE : 5 |
|-------------------------------------------------------------------------------------------------|----------------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|----------|
| Group Name                                                                                      | Control                                      | 750 ppm                             | 1500 ppm                            | 3000 ppm                            |          |
| Tumor rate                                                                                      | SITE : testis<br>TUMOR : interstitial cell t | unor"                               |                                     |                                     |          |
| Overall rates(a)<br>Adjusted rates(b)<br>Terminal rates(c)<br>Statistical analysis<br>Peto test | 46/50(92.0)<br>95.35<br>37/39(94.9)          | 39/50(78.0)<br>88.10<br>36/41(87.8) | 48/50(96.0)<br>97.96<br>40/41(97.6) | 48/50(96.0)<br>97.83<br>45/46(97.8) |          |
| Standard method(d)<br>Prevalence method(d)<br>Combined analysis(d)<br>Cochran-Armitage test(e)  | P =<br>P = 0.0649<br>P =<br>P = 0.0947       |                                     |                                     |                                     |          |
| Fisher Exact test(e)                                                                            |                                              | P = 0.3407                          | P = 0.4982                          | P = 0.4982                          |          |

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ANIMAL : RAT F344/DuCrj

(a): Number of tumor-bearing animals/number of animals examined at the site.

(b): Kaplan-Meire estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.

(c): Observed tumor incidence at terminal kill.

(d): Beneath the control incidence are the P-values associated with the trend test.

Standard method : Death analysis

Prevalence method : Incidental tumor test

Combined analysis : Death analysis + Incidental tumor test

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

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

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

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

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

# APPENDIX O 2

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

RAT : FEMALE

(2-YEAR STUDY)

| Group Name                                 | Control                                   | 750 ppm      | 1500 ppm              | 3000 ppm             |  |
|--------------------------------------------|-------------------------------------------|--------------|-----------------------|----------------------|--|
|                                            | SITE : spleen                             |              |                       |                      |  |
| Tumor rate                                 | TUMOR : mononuclear cell leukemia         |              |                       |                      |  |
| Overall rates(a)                           | 6/50( 12.0)                               | 4/50( 8.0)   | 5/50(10.0)            | 2/50/ 0.0)           |  |
| Adjusted rates(b)                          | 5,26                                      | 4,88         | 7.14                  | 3/50( 6.0)<br>2.56   |  |
| Terminal rates(c)                          | 2/38( 5.3)                                | 2/41( 4.9)   | 3/42(7.1)             | 1/39( 2.6)           |  |
| Statistical analysis                       |                                           |              |                       |                      |  |
| Peto test<br>Standard method(d)            | D 0. 6400                                 |              |                       |                      |  |
| Prevalence method(d)                       | P = 0.7468<br>P = 0.6840                  |              |                       |                      |  |
| Combined analysis(d)                       | P = 0.8002                                |              |                       |                      |  |
| Cochran-Armitage test(e)                   | P = 0.3582                                |              |                       |                      |  |
| Fisher Exact test(e)                       |                                           | P = 0.3944   | P = 0.4872            | P = 0.2728           |  |
|                                            | SITE : pituitary gland<br>TUMOR : adenoma |              |                       |                      |  |
| Tumor rate                                 |                                           |              |                       |                      |  |
| Overall rates(a)                           | 16/50( 32.0)                              | 23/50(46.0)  | 17/49(34.7)           | 12/50(24.0)          |  |
| Adjusted rates(b)                          | 34.21                                     | 46.34        | 30.43                 | 22.22                |  |
| Terminal rates(c)                          | 13/38( 34.2)                              | 19/41( 46.3) | 10/41(24.4)           | 7/39(17.9)           |  |
| Statistical analysis<br>Peto test          |                                           |              |                       |                      |  |
| Standard method(d)                         | P = 0.5565                                |              |                       |                      |  |
| Prevalence method(d)                       | P = 0.9104                                |              |                       |                      |  |
| Combined analysis(d)                       | P = 0.8973                                |              |                       |                      |  |
| Cochran-Armitage test(e)                   | P = 0.1607                                |              |                       |                      |  |
| Fisher Exact test(e)                       | · · · · · · · · · · · · · · · · · · ·     | P = 0.2231   | P = 0.5000            | P = 0.3253           |  |
|                                            | SITE : pituitary gland                    |              |                       |                      |  |
| Turner wete                                | TUMOR : adenoma, adenocarcinoma           |              |                       |                      |  |
| Tumor rate<br>Overall rates(a)             | 17/50(34.0)                               | 23/50( 46.0) | 17/40/ 24 7           |                      |  |
| Adjusted rates(b)                          | 34.21                                     | 46.34        | 17/49( 34.7)<br>30.43 | 12/50(24.0)<br>22.22 |  |
| Terminal rates(c)                          | 13/38( 34.2)                              | 19/41(46.3)  | 10/41(24.4)           | 7/39(17.9)           |  |
| Statistical analysis                       |                                           |              | · · · · · ·           | .,                   |  |
| Peto test                                  | D 0.0000                                  |              |                       |                      |  |
| Standard method(d)<br>Prevalence method(d) | P = 0.6832<br>P = 0.9206                  |              |                       |                      |  |
| Combined analysis(d)                       | P = 0.9208<br>P = 0.9304                  |              |                       |                      |  |
| Cochran-Armitage test(e)                   | P = 0.1156                                |              |                       |                      |  |
| Fisher Exact test(e)                       |                                           | P = 0.2696   | P = 0.4414            | P = 0.2725           |  |
|                                            |                                           |              |                       | ·                    |  |

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STUDY No. : 0267

ANIMAL : RAT F344/DuCrj SEX : FEMALE

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| SEX : FEMALE                                                                                                           | ·····                                                                                |                                                | 11-11 - 11-11-11-11-1-1-1          | PAGE :                            | 7 |
|------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|------------------------------------------------|------------------------------------|-----------------------------------|---|
| Group Name                                                                                                             | Control                                                                              | 750 ppm                                        | 1500 ppm                           | 3000 ppm                          |   |
|                                                                                                                        | SITE : thyroid<br>TUMOR : C-cell adenoma                                             |                                                |                                    |                                   |   |
| Tumor rate                                                                                                             |                                                                                      |                                                |                                    |                                   |   |
| Overall rates(a)                                                                                                       | 5/49( 10.2)                                                                          | 5/50( 10.0)                                    | 5/49( 10.2)                        | 6/50( 12.0)                       |   |
| Adjusted rates(b)                                                                                                      | 13.16                                                                                | 10.20                                          | 11.63                              | 15.38                             |   |
| Terminal rates(c)<br>Statistical analysis                                                                              | 5/38(13.2)                                                                           | 4/41( 9.8)                                     | 4/41( 9.8)                         | 6/39(15.4)                        |   |
| Peto test<br>Standard method(d)                                                                                        | P =                                                                                  |                                                |                                    |                                   |   |
| Prevalence method(d)                                                                                                   | P = 0.3189                                                                           |                                                |                                    |                                   |   |
| Combined analysis(d)                                                                                                   | P =                                                                                  |                                                |                                    |                                   |   |
| Cochran-Armitage test(e)                                                                                               | P = 0.7446                                                                           |                                                |                                    |                                   |   |
| Fisher Exact test(e)                                                                                                   |                                                                                      | P = 0.3592                                     | P = 0.3709                         | P = 0.4742                        |   |
| Tumor rate<br>Overall rates(a)<br>Adjusted rates(b)<br>Terminal rates(c)<br>Statistical analysis<br>Peto test          | SITE : thyroid<br>TUMOR : C-cell adenoma,C-cell<br>5/49(10.2)<br>13.16<br>5/38(13.2) | carcinoma<br>7/50(14.0)<br>14.63<br>6/41(14.6) | 5/49( 10.2)<br>11.63<br>4/41( 9.8) | 7/50(14.0)<br>15.38<br>6/39(15.4) |   |
| Standard method(d)<br>Prevalence method(d)<br>Combined analysis(d)<br>Cochran-Armitage test(e)<br>Fisher Exact test(e) | P = 0.1056<br>P = 0.4007<br>P = 0.2822<br>P = 0.6786                                 | P = 0.4195                                     | P = 0.3709                         | P = 0.4195                        |   |
|                                                                                                                        | SITE : adrenal gland<br>TUMOR : pheochromocytoma                                     |                                                |                                    |                                   |   |
| Tumor rate                                                                                                             |                                                                                      |                                                |                                    |                                   |   |
| Overali rates(a)                                                                                                       | 4/50( 8.0)                                                                           | 2/50( 4.0)                                     | 1/50( 2.0)                         | 0/50( 0.0)                        |   |
| Adjusted rates(b)                                                                                                      | 9.30                                                                                 | 4.88                                           | 2.38                               | 0.0                               |   |
| Terminal rates(c)<br>Statistical analysis                                                                              | 3/38( 7.9)                                                                           | 2/41( 4.9)                                     | 1/42( 2.4)                         | 0/39( 0.0)                        |   |
| Peto test<br>Standard method(d)                                                                                        | P =                                                                                  |                                                |                                    |                                   |   |
| Prevalence method(d)                                                                                                   | P = 0.9890                                                                           |                                                |                                    |                                   |   |
| Combined analysis(d)                                                                                                   | P =                                                                                  |                                                |                                    |                                   |   |
| Cochran-Armitage test(e)                                                                                               | P = 0.0319*                                                                          |                                                |                                    |                                   |   |
| Fisher Exact test(e)                                                                                                   |                                                                                      | P = 0.3574                                     | P = 0.1998                         | P = 0.0688                        |   |
|                                                                                                                        |                                                                                      |                                                |                                    |                                   |   |

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj SEX : FEMALE

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj SEX : FEMALE

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| Group Name                                       | Control                                            | 750 ppm             | 1500 ppm          | 3000 ppm           |
|--------------------------------------------------|----------------------------------------------------|---------------------|-------------------|--------------------|
|                                                  | SITE : adrenal gland                               |                     |                   |                    |
| Tumor rate                                       | TUMOR : pheochromocytoma, pheochrom                | NOCYTOMA: MALIGNANT |                   |                    |
| Overall rates(a)                                 | 5/50( 10.0)                                        | 2/50( 4.0)          | 1/50( 2.0)        | 0/50( 0.0)         |
| Adjusted rates(b)                                | 11.63                                              | 4.88                | 2,38              | 0.0                |
| Terminal rates(c)                                | 4/38(10.5)                                         | 2/41( 4.9)          | 1/42( 2.4)        | 0/39( 0.0)         |
| Statistical analysis                             |                                                    |                     |                   |                    |
| Peto test                                        |                                                    |                     |                   |                    |
| Standard method(d)                               | P =                                                |                     |                   |                    |
| Prevalence method(d)                             | P = 0.9960                                         |                     |                   |                    |
| Combined analysis(d)<br>Cochran-Armitage test(e) | P =<br>P = 0.0147*                                 |                     |                   |                    |
| Fisher Exact test(e)                             | F = 0.0147*                                        | P = 0.2425          | P = 0.1210        | P = 0.0360*        |
|                                                  |                                                    | 1 - 0.2425          | 1 - 0.1210        | F = 0.0500*        |
|                                                  | SITE : uterus<br>TUMOR : endometrial stromal polyp |                     |                   |                    |
| Tumor rate                                       |                                                    |                     |                   |                    |
| Overall rates(a)                                 | 8/50( 16.0)                                        | 12/50(24.0)         | 9/50(18.0)        | 15/50( 30.0)       |
| Adjusted rates(b)                                | 16.67                                              | 24.00               | 16.67             | 32.50              |
| Terminal rates(c)                                | 5/38(13.2)                                         | 8/41(19.5)          | 7/42(16.7)        | 12/39( 30.8)       |
| Statistical analysis                             |                                                    |                     |                   |                    |
| Peto test                                        |                                                    |                     |                   |                    |
| Standard method(d)<br>Preualence method(d)       | P = 0.6513<br>P = 0.0391*                          |                     |                   |                    |
| Combined analysis(d)                             | P = 0.0599                                         |                     |                   |                    |
| Cochran-Armitage test(e)                         | P = 0.1335                                         |                     |                   |                    |
| Fisher Exact test(e)                             |                                                    | P = 0.2846          | P = 0.4846        | P = 0.1384         |
|                                                  |                                                    |                     |                   |                    |
|                                                  | SITE : uterus                                      |                     |                   |                    |
|                                                  | TUMOR : endometrial stromal sarco                  | na                  |                   |                    |
| Tumor rate<br>Overall rates(a)                   | 1/50(20)                                           | 4/50/ 9.0)          | 0/50( 0.0)        |                    |
| Adjusted rates(b)                                | 1/50( 2.0)<br>0.0                                  | 4/50( 8.0)<br>4.88  | 0/50( 0.0)<br>0.0 | 1/50( 2.0)         |
| Terminal rates(c)                                | 0/38( 0.0)                                         | 2/41( 4.9)          | 0/42( 0.0)        | 2.56<br>1/39( 2.6) |
| Statistical analysis                             |                                                    | 2,11( 1.0)          | 0,12( 0.0)        | 1/03( 2.0)         |
| Peto test                                        |                                                    |                     |                   |                    |
| Standard method(d)                               | P = 0.8913                                         |                     |                   |                    |
| Prevalence method(d)                             | P = 0.3754                                         |                     |                   |                    |
| Combined analysis(d)                             | P = 0.7372                                         |                     |                   |                    |
| Cochran-Armitage test(e)<br>Fisher Exact test(e) | P = 0.4835                                         | D = 0.1000          | D 0 4050          |                    |
| FISHER EXACT TEST(0)                             |                                                    | P = 0.1998          | P = 0.4950        | P = 0.2475         |

| STUDY No. | : | 0267       |
|-----------|---|------------|
| ANTMAT    | • | RAT ESAN/I |

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: RAT F344/DuCrj : FEMALE ANIMAL

SEX

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| Group Name                                       | Control                      | 750 ppm             | 1500 ppm           | 3000 ppm          |
|--------------------------------------------------|------------------------------|---------------------|--------------------|-------------------|
|                                                  | SITE : mammary gland         |                     |                    |                   |
| Tumor rate                                       | TUMOR : fibroadenoma         |                     |                    |                   |
| Overall rates(a)                                 | 8/50(16.0)                   | 7/50(14.0)          | 5/50( 10.0)        | 6/50(12.0)        |
| Adjusted rates(b)                                | 17.95                        | 15.91               | 11.36              | 13.64             |
| Terminal rates(c)                                | 6/38(15.8)                   | 6/41(14.6)          | 4/42(9,5)          | 4/39(10.3)        |
| Statistical analysis                             |                              |                     |                    | -,,               |
| Peto test                                        | _                            |                     |                    |                   |
| Standard method(d)                               | P =                          |                     |                    |                   |
| Prevalence method(d)<br>Combined analysis(d)     | P = 0.6535<br>P =            |                     |                    |                   |
| Cochran-Armitage test(e)                         | P = 0.5224                   |                     |                    |                   |
| Fisher Exact test(e)                             | 1 - 0.0001                   | P = 0.4854          | P = 0.3141         | P = 0.4157        |
|                                                  | 1949-14                      |                     |                    |                   |
|                                                  | SITE : mammary gland         |                     |                    |                   |
| _                                                | TUMOR : adenocarcinoma       |                     |                    |                   |
| Tumor rate                                       |                              |                     |                    |                   |
| Overall rates(a)<br>Adjusted rates(b)            | 3/50( 6.0)<br>5.00           | 4/50( 8.0)<br>9.76  | 0/50( 0.0)         | 0/50( 0.0)        |
| Terminal rates(c)                                | 1/38(2.6)                    | 4/41(9.8)           | 0,0<br>0/42( 0.0)  | 0.0<br>0/39( 0.0) |
| Statistical analysis                             | 1,00( 1.0)                   | 1,11( 0.0)          | 0/42( 0:0)         | 0/33( 0.0/        |
| Peto test                                        |                              |                     |                    |                   |
| Standard method(d)                               | P = 0.9201 ?                 |                     |                    |                   |
| Prevalence method(d)                             | P = 0.9747                   |                     |                    |                   |
| Combined analysis(d)<br>Cochran-Armitage test(e) | P = 0.9904                   |                     |                    |                   |
| Fisher Exact test(e)                             | P = 0.0319*                  | P = 0.4895          | P = 0.1325         | D = 0.1995        |
|                                                  |                              | 1 - 0.4000          | F = 0.1325         | P = 0.1325        |
|                                                  | SITE : mammary gland         |                     |                    |                   |
|                                                  | TUMOR : fibroadenoma,adenoma |                     |                    |                   |
| Tumor rate                                       |                              |                     |                    |                   |
| Overall rates(a)                                 | 8/50(16.0)                   | 7/50(14.0)          | 5/50(10.0)         | 7/50(14.0)        |
| Adjusted rates(b)<br>Terminal rates(c)           | 17.95<br>6/38(15.8)          | 15.91<br>6/41(14.6) | 11.36<br>4/42(9.5) | 15.91             |
| Statistical analysis                             | 0,00( 10.0)                  | 0/41( 14.0)         | 4/42( 0.0)         | 5/39(12.8)        |
| Peto test                                        |                              |                     |                    |                   |
| Standard method(d)                               | P =                          |                     |                    |                   |
| Prevalence method(d)                             | P = 0.5254                   |                     |                    |                   |
| Combined analysis(d)                             | P =                          |                     |                    |                   |
| Cochran-Armitage test(e)<br>Fisher Exact test(e) | P = 0.7529                   | P = 0.4854          | D = 0.2141         | D 0. 1071         |
| TISHOL EXAUL LUST(U)                             |                              | r - V.4004          | P = 0.3141         | P = 0.4854        |

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

STUDY No. : 0267 ANIMAL : RAT F344/DuCrj SEX

: FEMALE

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| Group Name                     | Control                     | 750 ppm                               | 1500 ppm           | 3000 ppm            |  |
|--------------------------------|-----------------------------|---------------------------------------|--------------------|---------------------|--|
|                                | SITE : mammary gland        |                                       |                    |                     |  |
| lumor rate                     | TUMOR : fibroadenoma,adenom | a, adenocarcinoma                     |                    |                     |  |
| Overall rates(a)               | 11/50( 22.0)                | 10/50( 20.0)                          | 5/50( 10.0)        | 7/50/ 14 0)         |  |
| Adjusted rates(b)              | 22.50                       | 22.73                                 | 11.36              | 7/50(14.0)<br>15.91 |  |
| Terminal rates(c)              | 7/38(18.4)                  | 9/41(22.0)                            | 4/42(9.5)          | 5/39(12.8)          |  |
| Statistical analysis           | 1700(10,1)                  | 3/41( 22:0)                           | 4/42( 3.3)         | 5/59(12.6)          |  |
| Peto test                      |                             |                                       |                    |                     |  |
| Standard method(d)             | P = 0.9201 ?                |                                       |                    |                     |  |
| Prevalence method(d)           | P = 0.8077                  |                                       |                    |                     |  |
| Combined analysis(d)           | P = 0.8612                  |                                       |                    |                     |  |
| Cochran-Armitage test(e)       | P = 0.2092                  |                                       |                    |                     |  |
| Fisher Exact test(e)           |                             | P = 0.4833                            | P = 0.1300         | P = 0.2711          |  |
| - Alwaren                      |                             | · · · · · · · · · · · · · · · · · · · |                    |                     |  |
|                                | SITE : preputial/clitoral   | gland                                 |                    |                     |  |
| Rumana anala                   | TUMOR : adenoma             |                                       |                    |                     |  |
| 'umor rate<br>Overall rates(a) | 2/50( 4.0)                  | 4/50/ 8 0)                            |                    |                     |  |
| Adjusted rates(b)              | 4.08                        | 4/50( 8.0)<br>8.89                    | 2/50( 4.0)<br>4.76 | 1/50( 2.0)          |  |
| Terminal rates(c)              | 1/38( 2.6)                  | 3/41(7.3)                             | 2/42( 4.8)         | 2.56<br>1/39(2.6)   |  |
| Statistical analysis           | 1,00( 210)                  | 0/11( 1.0)                            | 2/42( 4.8)         | 1/39( 2.0)          |  |
| Peto test                      |                             |                                       |                    |                     |  |
| Standard method(d)             | P =                         |                                       |                    |                     |  |
| Prevalence method(d)           | P = 0.7630                  |                                       |                    |                     |  |
| Combined analysis(d)           | P =                         |                                       |                    |                     |  |
| Cochran-Armitage test(e)       | P = 0.3871                  |                                       |                    |                     |  |
| Fisher Exact test(e)           |                             | P = 0.3574                            | P = 0.3088         | P = 0.4926          |  |

(HPT360A)

(a): Number of tumor-bearing animals/number of animals examined at the site.

(b): Kaplan-Meire estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.

(c): Observed tumor incidence at terminal kill.

(d): Beneath the control incidence are the P-values associated with the trend test.

Standard method : Death analysis

Prevalence method : Incidental tumor test

Combined analysis : Death analysis + Incidental tumor test

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

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

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

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

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### APPENDIX P 1

### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY

RAT : MALE : ALL ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

#### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) ALL ANIMALS (0-105W)

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| )rgan        | Findings                   | Group Name<br>No. of Animals on Study | Contral<br>50 | 750 ppm<br>50 | 1500 ppm<br>50 | 3000 ppm<br>50 |
|--------------|----------------------------|---------------------------------------|---------------|---------------|----------------|----------------|
| Respirator   | y system]                  |                                       |               |               |                |                |
| lung         |                            |                                       | (50)          | (50)          | <b>(7 (</b> )  |                |
| luig         | leukemic cell infiltration |                                       | <50><br>3     | <50><br>1     | <50><br>3      | <50><br>0      |
|              | metastasis:adrenal tumor   |                                       | 2             | 0             | 0              | 0              |
|              | metastasis:subcutis tumor  |                                       | 2             | 0             | 0              | 0              |
|              | metastasis;vertebra tumor  |                                       | 0             | 1             | 0              | 0              |
| [Hematopoie  | tic system]                |                                       |               |               |                |                |
| xone marrow  |                            |                                       | <50>          | <50>          | <50>           | <50>           |
|              | leukemic cell infiltration |                                       | 1             | 0             | 2              | 0              |
| Lymph node   | leukemic cell infiltration |                                       | <50><br>2     | <50><br>0     | <50><br>0      | <50><br>0      |
|              | metastasis:adrenal tumor   |                                       | 1             | 0             | -              |                |
|              |                            |                                       | -             |               | 0              | 0              |
| thymus       | metastasis:adrenal tumor   |                                       | <50><br>1     | <50><br>0     | <50><br>0      | <50><br>0      |
| spleen       |                            |                                       | <50>          | <49>          | <50>           | <50>           |
|              | metastasis:subcutis tumor  |                                       | 1             | 0             | 0              | 0              |
| [Circulator: | y system]                  |                                       |               |               |                |                |
| heart        |                            |                                       | <50>          | <50>          | <50>           | <50>           |
|              | metastasis:adrenal tumor   |                                       | 1             | 0             | 0              | 0              |
|              | metastasis:subcutis tumor  |                                       | 1             | 0             | 0              | 0              |
| Digestive :  | system]                    |                                       |               |               |                |                |
| stomach      |                            |                                       | <50>          | <50>          | <50>           | <50>           |
|              | metastasis:subcutis tumor  |                                       | 1             | 0             | 0              | 0              |

(JPT150)

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

#### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) ALL ANIMALS (0-105W)

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|              |                            | Group Name              | Control   | 750 ppm   | 1500 ppm  | 3000 ppm  |
|--------------|----------------------------|-------------------------|-----------|-----------|-----------|-----------|
| rgan         | Findings                   | No. of Animals on Study | 50        | 50        | 50        | 50        |
| Digestive sy | stem]                      |                         |           |           |           |           |
| iver         | leukemic cell infiltration |                         | <50><br>4 | <50><br>1 | <50><br>3 | <50><br>1 |
|              | metastasis:subcutis tumor  |                         | 2         | 0         | 0         | 0         |
| ancreas      | metastasis:subcutis tumor  |                         | <50><br>1 | <50><br>0 | <50><br>0 | <50><br>0 |
| Finary syst  | em]                        |                         |           |           |           |           |
| idney        | leukemic cell infiltration |                         | <50><br>1 | <50><br>0 | <50><br>0 | <50><br>0 |
| indocrine sy | stem]                      |                         |           |           |           |           |
| ituitary     | leukemic cell infiltration |                         | <50><br>2 | <50><br>0 | <50><br>0 | <50><br>0 |
| irenal       | leukemic cell infiltration |                         | <50><br>2 | <50><br>0 | <50><br>1 | <50><br>0 |
| lervous syst | em]                        |                         |           |           |           |           |
| pinal cord   | leukemic cell infiltration |                         | <50><br>1 | <50><br>0 | <50><br>0 | <50><br>0 |
| Body cavitie | s]                         |                         |           |           |           |           |
| leura        | metastasis:subcutis tumor  |                         | <50><br>1 | <50><br>0 | <50><br>0 | <50><br>0 |
| eritoneum    | metastasis:subcutis tumor  |                         | <50><br>2 | <50><br>0 | <50><br>0 | <50><br>0 |

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### APPENDIX P 2

### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY

RAT : MALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

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# HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) SACRIFICED ANIMALS (105W)

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| SEX :          | MALE                                                                          |                                       |               |                                       |                                       | PAGE :         |
|----------------|-------------------------------------------------------------------------------|---------------------------------------|---------------|---------------------------------------|---------------------------------------|----------------|
| 0rgan          |                                                                               | Group Name<br>No. of Animals on Study | Control<br>39 | 750 ppm<br>41                         | 1500 ppm<br>41                        | 3000 ppm<br>46 |
| [Respiratory : | system]                                                                       |                                       |               |                                       |                                       |                |
| lung           | leukemic cell infiltration                                                    |                                       | <39><br>1     | <41><br>1                             | <41><br>2                             | <46><br>0      |
|                | metastasis:adrenal tumor                                                      |                                       | 1             | 0                                     | 0                                     | 0              |
|                | metastasis:vertebra tumor                                                     |                                       | 0             | 1                                     | 0                                     | 0              |
| [Hematopoieti  | c system]                                                                     |                                       |               |                                       |                                       |                |
| one marrow     | leukemic cell infiltration                                                    |                                       | <39><br>0     | <41><br>0                             | <41><br>1                             | <46><br>0      |
| thymus         | metastasis:adrenal tumor                                                      |                                       | <39><br>1     | <41><br>0                             | <41><br>0                             | <46><br>0      |
| [Digestive sy  | stem]                                                                         |                                       |               |                                       |                                       |                |
| liver          | leukemic cell infiltration                                                    |                                       | <39><br>1     | <41><br>1                             | <41><br>2                             | <46><br>1      |
| (a)<br>b       | a : Number of animals examined at the si<br>b : Number of animals with lesion | te                                    |               |                                       | · · · · · · · · · · · · · · · · · · · |                |
| (JPT150)       |                                                                               | ····                                  |               | · · · · · · · · · · · · · · · · · · · |                                       | BA             |

### APPENDIX P 3

### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY

RAT : MALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj

#### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

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|             |                            | Group Name<br>No. of Animals on Study | Control<br>11 | 750 ppm<br>9 | 1500 ppm<br>9 | 3000 ppm<br>4 |
|-------------|----------------------------|---------------------------------------|---------------|--------------|---------------|---------------|
| Organ       | Findings                   |                                       |               |              | ********      |               |
| Respiratory | system]                    |                                       |               |              |               |               |
| ung         | leukemic cell infiltration |                                       | <11><br>2     | < 9><br>0    | < 9><br>1     | < 4><br>0     |
|             | metastasis:adrenal tumor   |                                       | 1             | 0            | 0             | 0             |
|             | metastasis:subcutis tumor  |                                       | 2             | 0            | 0             | 0             |
| Hematopoiet | ic system]                 |                                       |               |              |               |               |
| one marrow  | leukemic cell infiltration |                                       | <11><br>1     | < 9><br>0    | < 9><br>1     | < 4><br>0     |
| vmph node   | leukemic cell infiltration |                                       | <11><br>2     | < 9><br>0    | < 9><br>0     | < 4><br>0     |
|             | metastasis:adrenal tumor   |                                       | 1             | 0            | 0             | 0             |
| oleen       | metastasis:subcutis tumor  |                                       | <11><br>1     | < 8><br>0    | < 9><br>0     | < 4><br>0     |
| Circulatory | system]                    |                                       |               |              |               |               |
| neart       | metastasis:adrenal tumor   |                                       | <11><br>1     | < 9><br>0    | < 9><br>0     | < 4><br>0     |
|             | metastasis:subcutis tumor  |                                       | 1             | 0            | 0             | 0             |
| Digestive s | ystem]                     |                                       |               |              |               |               |
| tomach      | mətastasis:subcutis tumor  |                                       | <11><br>1     | < 9><br>0    | < 9><br>0     | < 4><br>0     |
| iver        | leukemic cell infiltration |                                       | <11><br>3     | < 9>         | < 9><br>1     | < 4>          |

(JPT150)

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REPORT TYPE : A1 SEX : MALE

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| EX :          | MALE                       |                                       |               |              |               |               |  |  |
|---------------|----------------------------|---------------------------------------|---------------|--------------|---------------|---------------|--|--|
| rgan          | Findines                   | Group Name<br>No. of Animals on Study | Control<br>11 | 750 ppm<br>9 | 1500 ppm<br>9 | 3000 ppm<br>4 |  |  |
| Digestive sy  | stem]                      |                                       |               |              |               |               |  |  |
| liver         | metastasis:subcutis tumor  |                                       | <11><br>2     | < 9><br>0    | < 9><br>0     | < 4><br>0     |  |  |
| pancreas      | metastasis:subcutis tumor  |                                       | <11><br>1     | < 9><br>0    | < 9><br>0     | < 4><br>0     |  |  |
| (Urinary syst | em]                        |                                       |               |              |               |               |  |  |
| kidney        | leukemic cell infiltration |                                       | <11> 1        | < 9><br>0    | < 9><br>0     | < 4><br>0     |  |  |
| (Endocrine sy | stem]                      |                                       |               |              |               |               |  |  |
| pituitary     | leukemic cell infiltration |                                       | <11><br>2     | < 9><br>0    | < 9><br>0     | < 4><br>0     |  |  |
| adrenal       | leukemic cell infiltration |                                       | <11><br>2     | < 9><br>0    | < 9><br>1     | < 4><br>0     |  |  |
| [Nervous syst | em]                        |                                       |               |              |               |               |  |  |
| spinal cord   | leukemic cell infiltration |                                       | <11><br>1     | < 9><br>0    | < 9><br>0     | < 4><br>0     |  |  |
| [Body cavitie | s]                         |                                       |               |              |               |               |  |  |
| pleura        | metastasis:subcutis tumor  |                                       | <11><br>1     | < 9><br>0    | < 9><br>0     | < 4><br>0     |  |  |
| peritaneum    | metastasis:subcutis tumor  |                                       | <11><br>2     | < 9>         | < 9>          | < 4>          |  |  |

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj

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### APPENDIX P 4

### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY

RAT : FEMALE : ALL ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

# HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) ALL ANIMALS (0-105W)

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| Organ         | Findings                   | Group Name<br>No. of Animals on Study | Control<br>50 | 750 ppm<br>50 | 1500 ppm<br>50 | 3000 ppm<br>50 |
|---------------|----------------------------|---------------------------------------|---------------|---------------|----------------|----------------|
| [Respiratory  | system]                    |                                       |               |               |                |                |
| larynx        | metastasis:thyroid tumor   |                                       | <50><br>0     | <50><br>0     | <50><br>0      | <50><br>1      |
| tune          | leukemic cell infiltration |                                       | <50><br>5     | <50><br>3     | <50><br>3      | <50><br>3      |
|               | metastasis:adrenal tumor   |                                       | 1             | 0             | 0              | 0              |
|               | metastasis:thyroid tumor   |                                       | 0             | 0             | 0              | 1              |
|               | metastasis:subcutis tumor  |                                       | 0             | 0             | 0              | 1              |
| [Hematopoieti | c system]                  |                                       |               |               |                |                |
| xone marrow   | leukemic cell infiltration |                                       | <50><br>3     | <50><br>2     | <50><br>2      | <50><br>1      |
| ymph node     | leukemic cell infiltration |                                       | <50><br>0     | <50><br>1     | <50><br>1      | <50><br>0      |
|               | metastasis:thyroid tumor   |                                       | 0             | 0             | 0              | 1              |
| thymus        | leukemic cell infiltration |                                       | <50><br>0     | <50><br>2     | <50><br>2      | <50><br>1      |
| [Circulatory  | system]                    |                                       |               |               |                |                |
| art           | leukemic cell infiltration |                                       | <50><br>1     | <50><br>1     | <50><br>0      | <50><br>0      |
| [Digestive sy | rstem]                     |                                       |               |               |                |                |
| salivary gl   | leukemic cell infiltration |                                       | <50><br>0     | <50><br>1     | <50><br>0      | <50><br>0      |

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

#### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) ALL ANIMALS (0-105W)

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| )rgan        | Findings                   | Group Name<br>No. of Animals on Study | Control<br>50 | 750 ppm<br>50 | 1500 ppm<br>50 | 3000 ppm<br>50 |
|--------------|----------------------------|---------------------------------------|---------------|---------------|----------------|----------------|
|              |                            |                                       |               |               |                |                |
| (Digestive s | ystem]                     |                                       |               |               |                |                |
| tomach       | leukemic cell infiltration |                                       | <50><br>0     | <50><br>1     | <50><br>1      | <50><br>0      |
| iver         | leukemic cell infiltration |                                       | <50><br>6     | <50><br>4     | <50><br>5      | <50><br>2      |
| ancreas      | leukemic cell infiltration |                                       | <50><br>0     | <50><br>1     | <50><br>0      | <50><br>0      |
| Urinary sys  | rtem]                      |                                       |               |               |                |                |
| cidney       | leukemic cell infiltration |                                       | <50><br>0     | <50><br>1     | <50><br>1      | <50><br>0      |
| rin bladd    | leukemic cell infiltration |                                       | <50><br>0     | <50><br>0     | <50><br>1      | <50><br>0      |
| Endocrine s  | vstem]                     |                                       |               |               |                |                |
| oituitary    | leukemic cell infiltration |                                       | <50><br>0     | <50><br>1     | <50><br>1      | <50><br>0      |
| drenal       | leukemic cell infiltration |                                       | <50><br>0     | <50><br>2     | <50><br>0      | <50><br>0      |
| Reproductiv  | e system]                  |                                       |               |               |                |                |
| wary         | leukemic cell infiltration |                                       | <50><br>0     | <50><br>1     | <50><br>1      | <50><br>0      |
| terus        | leukemic cell infiltration |                                       | <50><br>0     | <50><br>1     | <50><br>1      | <50><br>0      |

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FENALE

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# HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) ALL ANIMALS (0-105W)

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| <b>\.</b>      |                                                                                 | Control<br>Mals on Study 50 | 750 ppm<br>50 | 1500 ppm<br>50 | 3000 ppm<br>50 |
|----------------|---------------------------------------------------------------------------------|-----------------------------|---------------|----------------|----------------|
| )rgan          | Findings                                                                        |                             |               |                |                |
| [Reproductive  | system]                                                                         |                             |               |                |                |
| yagina         | leukemic cell infiltration                                                      | <50><br>0                   | <50><br>1     | <50><br>1      | <50><br>0      |
| nammary gl     | leukemic cell infiltration                                                      | <50><br>1                   | <50><br>1     | <50><br>1      | <50><br>0      |
| (Nervous syste | m]                                                                              |                             |               |                |                |
| ain            | leukemic cell infiltration                                                      | <50><br>1                   | <50><br>0     | <50><br>1      | <50><br>0      |
| [Body cavities | ]                                                                               |                             |               |                |                |
| oleura         | leukemic cell infiltration                                                      | <50><br>0                   | <50><br>0     | <50><br>1      | <50><br>0      |
| <a>b</a>       | a : Number of animals examined at the site<br>b : Number of animals with lesion | ······                      |               |                |                |

### APPENDIX P 5

### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY

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

(2-YEAR STUDY)

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

| )rgan        | Findings                   | Group Name<br>No. of Animals on Study | Control<br>12 | 750 ppm<br>9 | 1500 ppm<br>8 | 3000 ppm<br>11 |
|--------------|----------------------------|---------------------------------------|---------------|--------------|---------------|----------------|
| Respiratory  | system]                    |                                       |               |              |               | ,,             |
| arynx        | metastasis:thyroid tumor   |                                       | <12><br>0     | < 9><br>0    | < 8><br>0     | <11> 1         |
| ung          | leukemic cell infiltration |                                       | <12><br>4     | < 9><br>2    | < 8><br>2     | <11><br>2      |
|              | metastasis:thyroid tumor   |                                       | 0             | 0            | 0             | 1              |
|              | metastasis:subcutis tumor  |                                       | 0             | 0            | 0             | 1              |
| [Hematopoiet | ic system]                 |                                       |               |              |               |                |
| xone marrow  | leukemic cell infiltration |                                       | <12><br>2     | < 9><br>2    | < 8><br>1     | <11><br>1      |
| ymph node    | leukemic cell infiltration |                                       | <12><br>0     | < 9><br>0    | < 8><br>1     | <11><br>0      |
|              | metastasis:thyroid tumor   |                                       | 0             | 0            | 0             | 1              |
| hymus        | leukemic cell infiltration |                                       | <12><br>0     | < 9><br>1    | < 8><br>2     | <11><br>1      |
| [Circulatory | y system]                  |                                       |               |              |               |                |
| neart        | leukemic cell infiltration |                                       | <12><br>1     | < 9><br>1    | < 8><br>0     | <11><br>0      |
| [Digestive s | vstem]                     |                                       |               |              |               |                |
| salivary gl  | leukemic cell infiltration |                                       | <12><br>0     | < 9><br>1    | < 8><br>0     | <11>           |

b b: Number of animals with lesion

PAGE : 3

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

PAGE: 4

| Organ                                                                                                                                                                   | Findings                   | Group Name<br>No. of Animals on Study | Control<br>12 | 750 ppm<br>9 | 1500 ppm<br>8 | 3000 ppm<br>11 |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|---------------------------------------|---------------|--------------|---------------|----------------|
| [D:                                                                                                                                                                     |                            |                                       |               |              |               |                |
| [Digestive s                                                                                                                                                            | ystem]                     |                                       |               |              |               |                |
| stomach                                                                                                                                                                 | leukemic cell infiltration |                                       | <12><br>0     | < 9><br>1    | < 8><br>1     | <11><br>0      |
| iver                                                                                                                                                                    | leukemic cell infiltration |                                       | <12><br>4     | < 9><br>2    | < 8><br>2     | <11><br>1      |
| [Urinary sys                                                                                                                                                            | tem]                       |                                       |               |              |               |                |
| <idney< td=""><td>leukemic cell infiltration</td><td></td><td>&lt;12&gt;<br/>0</td><td>&lt; 9&gt;<br/>1</td><td>&lt; 8&gt;<br/>1</td><td>&lt;11&gt;<br/>0</td></idney<> | leukemic cell infiltration |                                       | <12><br>0     | < 9><br>1    | < 8><br>1     | <11><br>0      |
| urin bladd                                                                                                                                                              | leukemic cell infiltration |                                       | <12><br>0     | < 9><br>0    | < 8><br>1     | <11><br>0      |
| Endocrine s                                                                                                                                                             | vstem]                     |                                       |               |              |               |                |
| pituitary                                                                                                                                                               | leukemic cell infiltration |                                       | <12><br>0     | < 9><br>1    | < 8><br>1     | <11><br>0      |
| adrenal                                                                                                                                                                 | leukemic cell infiltration |                                       | <12><br>0     | < 9><br>1    | < 8><br>0     | <11><br>0      |
| [Reproductiu                                                                                                                                                            | e system]                  |                                       |               |              |               |                |
| DVary                                                                                                                                                                   | leukemic cell infiltration |                                       | <12><br>0     | < 9><br>1    | < 8><br>1     | <11><br>0      |
| uterus                                                                                                                                                                  | leukemic cell infiltration |                                       | <12><br>0     | < 9><br>1    | < 8><br>1     | <11><br>0      |
| Jagina                                                                                                                                                                  | leukemic cell infiltration |                                       | <12><br>0     | < 9>         | < 8><br>1     | <11><br>0      |

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STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

PAGE: 5

| Organ         |                                                                                 | oup Name<br>. of Animals on Study | Control<br>12                                                                                                                                                                                                                                                                 | 750 ppm<br>9 | 1500 ppm<br>8 | 3000 ppm<br>11 |
|---------------|---------------------------------------------------------------------------------|-----------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|---------------|----------------|
| [Reproductive | a svetam]                                                                       |                                   |                                                                                                                                                                                                                                                                               |              |               |                |
|               |                                                                                 |                                   |                                                                                                                                                                                                                                                                               |              |               |                |
| mammary gl    | leukemic cell infiltration                                                      |                                   | <12><br>0                                                                                                                                                                                                                                                                     | < 9><br>1    | < 8><br>1     | <11><br>0      |
| [Nervous syst | tem]                                                                            |                                   |                                                                                                                                                                                                                                                                               |              |               |                |
| brain         | leukemic cell infiltration                                                      |                                   | <12><br>1                                                                                                                                                                                                                                                                     | < 9><br>0    | < 8><br>1     | <11><br>0      |
| [Body cavitie | [26                                                                             |                                   |                                                                                                                                                                                                                                                                               |              |               |                |
| pleura        | leukemic cell infiltration                                                      |                                   | <12><br>0                                                                                                                                                                                                                                                                     | < 9><br>0    | < 8><br>1     | <11><br>0      |
| <a>b</a>      | a : Number of animals examined at the site<br>b : Number of animals with lesion |                                   | , ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, ,, , ,, , ,, , ,, , ,, , ,, , ,, , ,, , , , , , , , , , , , , , , , , , , , |              |               |                |

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### APPENDIX P 6

### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY

RAT : FEMALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0267 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

#### HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) SACRIFICED ANIMALS (105W)

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| SEX           | : FEMALE                                                               |                                       |               |               |                | PAGE :         |
|---------------|------------------------------------------------------------------------|---------------------------------------|---------------|---------------|----------------|----------------|
| Organ         | Findings                                                               | Group Name<br>No. of Animals on Study | Control<br>38 | 750 ppm<br>41 | 1500 ppm<br>42 | 3000 ppm<br>39 |
| [Respiratory  | system]                                                                |                                       |               |               |                |                |
| lung          | leukemic cell infiltration                                             |                                       | <38><br>1     | <41><br>1     | <42><br>1      | <39><br>1      |
|               | metastasis:adrenal tumor                                               |                                       | 1             | 0             | 0              | 0              |
| [Hematopoiet  | ic system]                                                             |                                       |               |               |                |                |
| bone marrow   | leukemic cell infiltration                                             |                                       | <38><br>1     | <41><br>0     | <42><br>1      | <39><br>0      |
| lymph node    | leukemic cell infiltration                                             |                                       | <38><br>0     | <41><br>1     | <42><br>0      | <39><br>0      |
| thymus        | leukemic cell infiltration                                             |                                       | <38><br>0     | <41><br>1     | <42><br>0      | <39><br>0      |
| (Digestive s  | vstem]                                                                 |                                       |               |               |                |                |
| liver         | leukemic cell infiltration                                             |                                       | <38><br>2     | <41><br>2     | <42><br>3      | <39><br>1      |
| pancreas      | leukemic cell infiltration                                             |                                       | <38><br>0     | <41><br>1     | <42><br>0      | <39><br>0      |
| [Endocrine s) | vstem]                                                                 |                                       |               |               |                |                |
| adrenal       | leukemic cell infiltration                                             |                                       | <38><br>0     | <41><br>1     | <42><br>0      | <39><br>0      |
| [Reproductive | ə system]                                                              |                                       |               |               |                |                |
| mammary gl    | leukemic cell infiltration                                             |                                       | <38><br>1     | <41><br>0     | <42><br>0      | <39><br>0      |
| <a>b</a>      | a : Number of animals examined at<br>b : Number of animals with lesion | the site                              |               |               |                |                |

b b: Number of animals with lesion

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APPENDIX Q 1

IDENTITY OF GLYOXAL IN THE 2-YEAR DRINKING WATER STUDY

IDENTITY OF GLYOXAL IN THE 2-YEAR DRINKING WATER STUDY

Test Substance: Glyoxal (Wako Pure Chemical Industries, LTD.)A. Lot No.: CAK4487

1. Spectral data

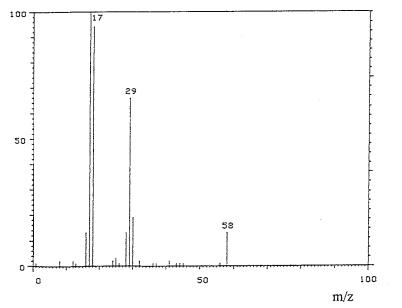
)

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Mass Spectrometry

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

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

| <u>Literature Values</u><br>Fragment Peak (m/z) |
|-------------------------------------------------|
| 17<br>29<br>58                                  |
|                                                 |

Results: The mass spectrum was consistent with literature spectrum.

(\*S. R. Heller and G. W. A. Milne (1978) EPA/NIH Mass spectral data base. Nat. Stand. Ref. Data Ser., Nat. Bur. Stand. (U.S.), 63, Vol. 1, pp. 7)

2. Conclusions: The test substance was identified as glyoxal, by the mass spectrum.

B. Lot No.

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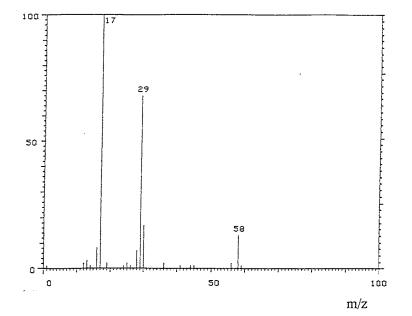
)

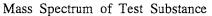
1. Spectral data

Mass Spectrometry

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

Ionization Voltage : 70eV





Results: The mass spectrum was consistent with literature spectrum.

(\*S. R. Heller and G. W. A. Milne (1978) EPA/NIH Mass spectral data base. Nat. Stand. Ref. Data Ser., Nat. Bur. Stand. (U.S.), 63, Vol. 1, pp. 7)

2. Conclusions: The test substance was identified as glyoxal, by the mass spectrum.

- C. Lot No.
- : SKE5515
- 1. Spectral data

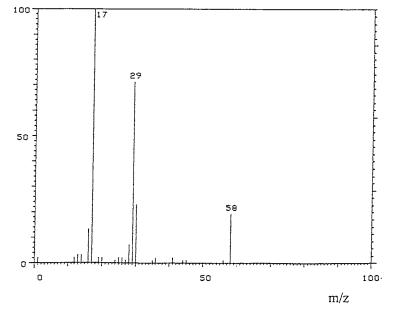
)

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Mass Spectrometry

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

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

| Determined Values   | Literature Values <sup>*</sup> |
|---------------------|--------------------------------|
| Fragment Peak (m/z) | Fragment Peak (m/z)            |
|                     |                                |
| 17                  | 17                             |
| 29                  | 29                             |
| 58                  | 58                             |
|                     |                                |

Results: The mass spectrum was consistent with literature spectrum.

(\*S. R. Heller and G. W. A. Milne (1978) EPA/NIH Mass spectral data base. Nat. Stand. Ref. Data Ser., Nat. Bur. Stand. (U.S.), 63, Vol. 1, pp. 7)

2. Conclusions: The test substance was identified as glyoxal, by the mass spectrum.

APPENDIX Q 2

STABILITY OF GLYOXAL IN THE 2-YEAR DRINKING WATER STUDY

|               |               | Target Concer          | ntration     |
|---------------|---------------|------------------------|--------------|
| Date Prepared | Date Analyzed | 750°                   | 3000         |
| 1994.08.29    | 1994.08.29    | 773 (100) <sup>b</sup> | 3145 (100)   |
|               | 1994.09.02°   | 759 ( 98.2)            | 3096 ( 98.4) |
|               | 1994.09.06°   | 728 ( 94.2)            | 2955 ( 94.0) |

### STABILITY OF GLYOXAL IN FORMULATED WATER IN THE 2-YEAR DRINKING WATER STUDY

|               |                         | Target Conce           | ntration    |
|---------------|-------------------------|------------------------|-------------|
| Date Prepared | Date Analyzed           | 750ª                   | 3000        |
| 1994.12.02    | 1994.12.02              | 773 (100) <sup>b</sup> | 3107 (100)  |
|               | 1994.12.16 <sup>c</sup> | 717 ( 92.8)            | 3077 (99.0) |

å ppm

<sup>b</sup> % (Percentage were based on the concentration on date of preparation.)

<sup>c</sup> Animal room samples

Analytical method : The samples were analyzed by the GC.

| Instrument | : Hewlett Packard 5890A Gas Chromatograph     |                              |
|------------|-----------------------------------------------|------------------------------|
| Column     | : Methyl Silicone (0.2 mm $\phi \times 25$ m) | Column Temperature: 140 °C   |
| Flow Rate  | : 0.7 mL/min                                  | Injection Volume : $1 \mu L$ |
| Detector   | : FID (Flame Ionization Detector)             |                              |
|            |                                               |                              |

Pre-Treatment : Glyoxal was allowed to react with quinoxaline, and analyzed. First, 50% hydroxylammonium chloride (0.02 mL), 36% hydrochloric acid (0.1 mL), 4% o-phenylene diamine dihydrochloride (0.05 mL) were added to a glyoxal solution (1 mL). This mixture was stirred at 75 °C for 0.5 hr. Then, this solution was extracted with ethyl acetate (2 mL) and analyzed.

APPENDIX R 1

CONCENTRATION OF GLYOXAL IN FORMULATED WATER IN THE 2-YEAR DRINKING WATER STUDY

| Target Concentration |                          |              |              |  |
|----------------------|--------------------------|--------------|--------------|--|
| Date Analyzed        | 750ª                     | 1500         | 3000         |  |
| 1994.09.09           | 755 (100.7) <sup>b</sup> | 1512 (100.8) | 3038 (101.3) |  |
| 1994.12.02           | 773 (103.1)              | 1549 (103.3) | 3107 (103.6) |  |
| 1995.02.17           | 745 ( 99.3)              | 1654 (110.3) | 3366 (112.2) |  |
| 1995.05.23           | 727 ( 96.9)              | 1485 ( 99.0) | 3007 (100.2) |  |
| 1995.08.15           | 780 (104.0)              | 1571 (104.7) | 3194 (106.5) |  |
| 1995.11.07           | 804 (107.2)              | 1526 (101.7) | 3126 (104.2) |  |
| 1996.01.30           | 768 (102.4)              | 1565 (104.3) | 3144 (104.8) |  |
| 1996.04.23           | 806 (107.5)              | 1614 (107.6) | 3173 (105.8) |  |
| 1996.07.16           | 752 (100.3)              | 1548 (103.2) | 3087 (102.9) |  |

CONCENTRATION OF GLYOXAL IN FORMULATED WATER IN THE 2-YEAR DRINKING WATER STUDY

° ppm

ь %

Analytical method: The samples were analyzed by the GC.

| Instrument<br>Column<br>Flow Rate | : Hewlett Packard 5890A Gas Chromatograph<br>: Methyl Silicone (0.2 mm $\phi \times 25$ m)<br>: 0.7 mL/min | Column Temperature: 140 °C<br>Injection Volume : 1 μL |
|-----------------------------------|------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|
| Detector                          | : FID (Flame Ionization Detector)                                                                          | injection volume : 1 µL                               |

Pre-Treatment : Glyoxal was allowed to react with quinoxaline, and analyzed. First, 50% hydroxylammonium chloride (0.02 mL), 36% hydrochloric acid (0.1 mL), 4% o-phenylene diamine dihydrochloride (0.05 mL) were added to a glyoxal solution (1 mL). This mixture was stirred at 75 °C for 0.5 hr. Then, this solution was extracted with ethyl acetate (2 mL) and analyzed.

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### APPENDIX R 2

### STABILITY OF GLYOXAL IN FORMULATED WATER IN THE

2-YEAR DRINKING WATER STUDY

#### STABILITY OF GLYOXAL IN THE 2-YEAR DRINKING WATER STUDY

: Glyoxal (Wako Pure Chemical Industries, LTD.) Test Substance

A. Lot No. : CAK4487

1. Sample : This lot was used from 1994.9.9 to 1995.8.18. Test substance was stored in the dark place at room temperature.

#### 2. Gas Chromatography

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| Instrument         | : Hewlett Packard 5890A Gas Chromatograph                                                                                                                                                                                                                                                                                                                                  |
|--------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Column             | : Methyl Silicone (0.2 mm $\phi$ × 25 m)                                                                                                                                                                                                                                                                                                                                   |
| Column Temperature | : 140 °C                                                                                                                                                                                                                                                                                                                                                                   |
| Flow Rate          | : 0.7 mL/min                                                                                                                                                                                                                                                                                                                                                               |
| Detector           | : FID (Flame Ionization Detector)                                                                                                                                                                                                                                                                                                                                          |
| Injection Volume   | :1 μL                                                                                                                                                                                                                                                                                                                                                                      |
| Pre-Treatment      | : Glyoxal was allowed to react with quinoxaline, and analyzed. First, 50% hydroxylammonium chloride (0.02 mL), 36% hydrochloric acid (0.1 mL), 4% o-phenylene diamine dihydrochloride (0.05 mL) were added to a glyoxal solution (1 mL). This mixture was stirred at 75 $^{\circ}$ C for 0.5 hr. Then, this solution was extracted with ethyl acetate (2 mL) and analyzed. |

| Date<br>(date analyzed) | Peak No. | Retention Time<br>(min)       | Area*<br>(%) |
|-------------------------|----------|-------------------------------|--------------|
| 1994.09.05              | 1<br>2   | 1.293 (Solvent Peak)<br>2.03  | 100          |
| 1995.08.28              | 1<br>2   | 1.292 (Solvent Peak)<br>2.028 | 100          |

\* The solvent peak was excluded from the area calculation.

Results: Gas chromatography indicated one major peak (peak No.2) and solvent peak (peak No.1) analyzed at 1994.9.5 and one major peak (peak No.2) and solvent peak (peak No.1) analyzed at 1995.8.28. No new trace impurity peak in the test substance analyzed at 1995.8.28 was detected.

3. Conclusions: The test substance was stable for about 1 year in the dark place at room temperature.

B. Lot No. : SKQ5736

- 1. Sample : This lot was used from 1995.8.18 to 1996.3.8. Test substance was stored in the dark at room temperature.
- 2. Gas Chromatography

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| Instrument         | : Hewlett Packard 5890A Gas Chromatograph                                                                                                                                                                                                                                                                                                                  |
|--------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Column             | : Methyl Silicone (0.2mm $\phi \times 25m$ )                                                                                                                                                                                                                                                                                                               |
| Column Temperature | : 140° C                                                                                                                                                                                                                                                                                                                                                   |
| Flow Rate          | : 0.7 mL/min                                                                                                                                                                                                                                                                                                                                               |
| Detector           | : FID (Flame Ionization Detector)                                                                                                                                                                                                                                                                                                                          |
| Injection Volume   | : 1 μL                                                                                                                                                                                                                                                                                                                                                     |
| Pre-Treatment      | : Glyoxal was allowed to react with quinoxaline, and analyzed. First, 50% hydroxylammonium chloride (0.02mL), 36% hydrochloric acid (0.1mL), 4% o-phenylene diamine dihydrochloride (0.05mL) were added to a glyoxal solution (1mL). This mixture was stirred at 75°C for 0.5 hr. Then, this solution was extracted with ethyl acetate (2mL) and analyzed. |

| Date<br>(date analyzed) | Peak No. | Retention Time<br>(min) | Area*<br>(%) |
|-------------------------|----------|-------------------------|--------------|
| 1995.08.15              | 1        | 1.227 (Solvent peak)    |              |
|                         | 2        | 2.055                   | 100          |
| 1996.03.15              | 1        | 1.227 (Solvent peak)    |              |
|                         | 2        | 2.055                   | 100          |

\* The solvent peak was excluded from the area calculation.

- Results: Gas chromatography indicated one major peak (peak No.2) and solvent peak (peak No.1) analyzed at 1995.8.15 and one major peak (peak No.2) and solvent peak (peak No.1) analyzed at 1996.3.15. No new trace impurity peak in the test substance analyzed at 1996.3.15 was detected.
- 3. Conclusions: The test substance was stable for about 7 months in the dark at room temperature.

C. Lot No. : SKE5515

- 1. Sample : This lot was used from 1996.3.8 to 1996.9.13. Test substance was stored in the dark at room temperature.
- 2. Gas Chromatography

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| Instrument         | : Hewlett Packard 5890A Gas Chromatograph                                                                                                                                                                                                                                                                                                                  |
|--------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Column             | : Methyl Silicone (0.2mm $\phi \times 25$ m)                                                                                                                                                                                                                                                                                                               |
| Column Temperature | : 140° C                                                                                                                                                                                                                                                                                                                                                   |
| Flow Rate          | : 0.7 mL/min                                                                                                                                                                                                                                                                                                                                               |
| Detector           | : FID (Flame Ionization Detector)                                                                                                                                                                                                                                                                                                                          |
| Injection Volume   | :1 μL                                                                                                                                                                                                                                                                                                                                                      |
| Pre-Treatment      | : Glyoxal was allowed to react with quinoxaline, and analyzed. First, 50% hydroxylammonium chloride (0.02mL), 36% hydrochloric acid (0.1mL), 4% o-phenylene diamine dihydrochloride (0.05mL) were added to a glyoxal solution (1mL). This mixture was stirred at 75°C for 0.5 hr. Then, this solution was extracted with ethyl acetate (2mL) and analyzed. |

| Date<br>(date analyzed) | Peak No. | Retention Time<br>(min)       | Area*<br>(%) |  |
|-------------------------|----------|-------------------------------|--------------|--|
| 1996.02.13              | 1<br>2   | 1.207 (Solvent peak)<br>2.008 | 100          |  |
| 1996.10.15              | 1<br>2   | 1.207 (Solvent peak)<br>2.01  | 100          |  |

\* The solvent peak was excluded from the area calculation.

- Results: Gas chromatography indicated one major peak (peak No.2) and solvent peak (peak No.1) analyzed at 1996.2.13 and one major peak (peak No.2) and solvent peak (peak No.1) analyzed at 1996.10.15. No new trace impurity peak in the test substance analyzed at 1996.10.15 was detected.
- 3. Conclusions: The test substance was stable for about 8 months in the dark at room temperature.

### APPENDIX S 1

# METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE 2-YEAR DRINKING WATER STUDY OF GLYOXAL

### METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE 2-YEAR DRINKING WATER STUDY OF GLYOXAL

| Item                                                                   | Method                                                                  |
|------------------------------------------------------------------------|-------------------------------------------------------------------------|
| Hematology                                                             |                                                                         |
| Red blood cell (RBC)                                                   | Light scattering method <sup>1)</sup>                                   |
| Hemoglobin (Hgb)                                                       | Cyanmethemoglobin method <sup>1)</sup>                                  |
| Hematocrit (Hct)                                                       | Calculated as RBC $\times$ MCV/10 <sup>1)</sup>                         |
| Mean corpuscular volume (MCV)                                          | Light scattering method <sup>1)</sup>                                   |
| Mean corpuscular hemoglobin (MCH)                                      | Calculated as Hgb/RBC $\times$ 10 <sup>1)</sup>                         |
| Mean corpuscular hemoglobin concentration (MCHC)                       | Calculated as Hgb/Hct $\times 100^{1}$                                  |
| Platelet                                                               | Light scattering method <sup>1)</sup>                                   |
| White blood cell (WBC)                                                 | Light scattering method <sup>1)</sup>                                   |
| Differential WBC                                                       | Pattern recognition method <sup>2)</sup>                                |
|                                                                        | (May-Grunwald-Giemsa staining)                                          |
| Biochemistry                                                           |                                                                         |
| Total protein (TP)                                                     | Biuret method <sup>3)</sup>                                             |
| Albumin (Alb)                                                          | BCG method <sup>3)</sup>                                                |
| A/G ratio                                                              | Calculated as Alb/ $(TP - Alb)^{3}$                                     |
| T-bilirubin                                                            | Alkaline azobilirubin method "                                          |
| Glucose                                                                | Enzymatic method (GLK·G-6-PDH) <sup>3)</sup>                            |
| T-cholesterol                                                          | Enzymatic method (CE·COD·POD)                                           |
| Triglyceride                                                           | Enzymatic method (LPL $\cdot$ GK $\cdot$ GPO $\cdot$ POD) <sup>3)</sup> |
| Phospholipid                                                           | Enzymatic method (PLD·COD·POD) <sup>3)</sup>                            |
| Glutamic oxaloacetic transaminase (GOT)                                | $UV \cdot Rate method^{3}$                                              |
| Glutamic pyruvic transaminase (GPT)                                    | $UV \cdot Rate method^{3}$                                              |
| Lactate dehydrogenase (LDH)                                            | UV•Rate method <sup>3)</sup>                                            |
| Alkaline phosphatase (ALP)                                             | p-Nitrophenylphosphate method <sup>3)</sup>                             |
| $\gamma$ -Glutamyl transpeptidase ( $\gamma$ -GTP)                     | L- $\gamma$ -Glutamyl-p-nitroanilide method <sup>3)</sup>               |
| Creatine phosphokinase (CPK)                                           | UV•Rate method <sup>37</sup>                                            |
| Urea nitrogen                                                          | Enzymatic method (Urease $\cdot$ GLDH) <sup>3)</sup>                    |
| Creatinine                                                             | Jaffe method <sup>3)</sup>                                              |
| Sodium                                                                 | Ion selective electrode method <sup>3)</sup>                            |
| Potassium                                                              | Ion selective electrode method <sup>3)</sup>                            |
| Chloride                                                               | Ion selective electrode method <sup>3)</sup>                            |
| Calcium                                                                | OCPC method <sup>3)</sup>                                               |
| Inorganic phosphorus                                                   | Enzymatic method (PNP·XOD·POD) <sup>3)</sup>                            |
| Urinalysis                                                             |                                                                         |
| pH,Protein,Glucose,Ketone body,Bilirubin,Occult blood,<br>Urobilinogen | Urinalysis reagent paper method 4)                                      |

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

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

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

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

### APPENDIX S 2

# UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-YEAR DRINKING WATER STUDY OF GLYOXAL

### UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-YEAR DRINKING WATER STUDY OF GLYOXAL

| Item                                               | Unit                  | Decimal<br>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                                           | $\times 10^3 / \mu L$ | 0                |
| White blood cell (WBC)                             | $\times 10^3 / \mu L$ | 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 transminase (GOT)             | IU/L                  | 0                |
| Glutamic pyruvic transaminase (GPT)                | IU/L                  | 0                |
| Lactate dehydrogenase (LDH)                        | IU/L                  | 0                |
| Alkaline phosphatase (ALP)                         | IU/L                  | 0                |
| $\gamma$ -Glutamyl transpeptidase ( $\gamma$ -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                                            | mg/dL                 | 1                |
| Inorganic phosphorus                               | mg/dL                 | 1                |

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