グリシドールのラットを用いた 吸入によるがん原性試験報告書

試験番号:0342

# APPENDIX

### APPENDICES

- APPENDIX A 1 CLINICAL OBSERVATION : SUMMARY, RAT : MALE (2-YEAR STUDY)
- APPENDIX A 2 CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE (2-YEAR STUDY)
- APPENDIX B 1 BODY WEIGHT CHANGES : SUMMARY, RAT : MALE (2-YEAR STUDY)
- APPENDIX B 2 BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE (2-YEAR STUDY)

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- APPENDIX C 1 FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE (2-YEAR STUDY)
- APPENDIX C 2 FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE (2-YEAR STUDY)
- APPENDIX D 1 HEMATOLOGY : SUMMARY, RAT : MALE (2-YEAR STUDY)
- APPENDIX D 2 HEMATOLOGY : SUMMARY, RAT : FEMALE (2-YEAR STUDY)
- APPENDIX E 1BIOCHEMISTRY : SUMMARY, RAT : MALE (2-YEAR STUDY)APPENDIX E 2BIOCHEMISTRY : SUMMARY, RAT : FEMALE (2-YEAR STUDY)
- APPENDIX F 1 URINALYSIS : SUMMARY, RAT : MALE (2-YEAR STUDY)
- APPENDIX F 2 URINALYSIS : SUMMARY, RAT : FEMALE (2-YEAR STUDY)
- APPENDIX G 1 GROSS FINDINGS : SUMMARY, RAT : MALE : ALL ANIMALS (2-YEAR STUDY)
- APPENDIX G 2 GROSS FINDINGS : SUMMARY, RAT : MALE : DEAD AND MORIBUND ANIMALS (2-YEAR STUDY)
- APPENDIX G 3 GROSS FINDINGS : SUMMARY, RAT : MALE :
  - SACRIFICED ANIMALS (2-YEAR STUDY)
- APPENDIX G 4 GROSS FINDINGS : SUMMARY, RAT : FEMALE : ALL ANIMALS (2-YEAR STUDY)

## APPENDICES (CONTINUED)

- APPENDIX G 5 GROSS FINDINGS : SUMMARY, RAT : FEMALE : DEAD AND MORIBUND ANIMALS (2-YEAR STUDY) APPENDIX G 6 GROSS FINDINGS : SUMMARY, RAT : FEMALE :
  - SACRIFICED ANIMALS ( 2-YEAR STUDY )

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- APPENDIX H 1 ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE (2-YEAR STUDY)
- APPENDIX H 2 ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE (2-YEAR STUDY)
- APPENDIX I 1 ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE (2-YEAR STUDY)
- APPENDIX I 2 ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE (2-YEAR STUDY)
- APPENDIX J 1 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY, RAT : MALE : ALL ANIMALS (2-YEAR STUDY)
- APPENDIX J 2 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY, RAT : MALE : DEAD AND MORIBUND ANIMALS (2-YEAR STUDY)
- APPENDIX J 3 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY, RAT : MALE : SACRIFICED ANIMALS (2-YEAR STUDY)
- APPENDIX J 4 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY, RAT : FEMALE : ALL ANIMALS (2-YEAR STUDY)
- APPENDIX J 5 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY, RAT : FEMALE : DEAD AND MORIBUND ANIMALS (2-YEAR STUDY)
- APPENDIX J 6 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS (2-YEAR STUDY)

# APPENDICES (CONTINUED)

- APPENDIX K 1 NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED, RAT : MALE (2-YEAR STUDY) APPENDIX K 2 NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED, RAT : FEMALE (2-YEAR STUDY)
- APPENDIX L 1 HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS : SUMMARY, RAT : MALE (2-YEAR STUDY)
- APPENDIX L 2 HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS : SUMMARY, RAT : FEMALE ( 2-YEAR STUDY )
- APPENDIX M 1 NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS, RAT : MALE ( 2-YEAR STUDY )
- APPENDIX M 2 NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS, RAT : FEMALE (2-YEAR STUDY)
- APPENDIX N 1 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY, RAT : MALE : ALL ANIMALS (2-YEAR STUDY)
- APPENDIX N 2 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY, RAT : MALE : DEAD AND MORIBUND ANIMALS (2-YEAR STUDY)
- APPENDIX N 3 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY, RAT : MALE : SACRIFICED ANIMALS (2-YEAR STUDY)

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APPENDIX N 4 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY, RAT : FEMALE : ALL ANIMALS (2-YEAR STUDY)

- APPENDIX N 5 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY,RAT:FEMALE: DEAD AND MORIBUND ANIMALS (2-YEAR STUDY)
- APPENDIX N 6 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS (2-YEAR STUDY)

# APPENDICES (CONTINUED)

- APPENDIX O 1 IDENTITY AND IMPURITY OF GLYCIDOL IN THE 2-YEAR INHALATION STUDY
- APPENDIX O 2 STABILITY OF GLYCIDOL IN THE 2-YEAR INHALATION STUDY

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- APPENDIX P 1 CONCENTRATION OF GLYCIDOL IN THE INHALATION CHAMBER OF THE 2-YEAR INHALATION STUDY
   APPENDIX P 2 ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-YEAR INHALATION STUDY OF GLYCIDOL
- APPENDIX Q METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-YEAR INHALATION STUDY OF GLYCIDOL

# APPENDIX A 1

# CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(2-YEAR STUDY)

#### SEX : MALE

PAGE : 1

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
		1	1	1	1	1	1	1	1	1	1	1	12-7	13-7	14-7 1
ЕАТН	0	<u> </u>													
	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ORIBUND SACRIFICE	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	õ	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	ō	õ	Ő	õ	0
OCOMOTOR MOVEMENT DECR	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	Õ	Ő	õ	0	0	0	0	0
	10 ppm	0	0	0	0	õ	õ	Õ	õ	0	0	0	0	0	
	30 ppm	0	0	0	0	õ	õ	0 0	0	0	0	0	0	0	0 0
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	10 ppm	0	0	0	0	Õ	Õ	0	0	0	-	0	0	0	0
	30 ppm	0	0	Ő	0	Õ	0	0	0	0	0 0	0	0 0	0	0 0
UNCHBACK POSITION	0 ppm	0	0	0	0	0	0	0	0	<u> </u>	0				
	3 ppm	õ	õ	Ő	õ	0	0	0	-	0	0	0	0	0	0
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ARALYTIC GAIT	0 ppm	0	0	0	0	•				-	-			·	v
	3 ppm	0	0	0 0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0		0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0 0	0 0	0 0	0 0	0 0	0 0	0	0	0 0	0 0	0	0 0
ASTING	0 ppm	0	0	0	0			-		-			U	U	U
	3 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
	10 ppm 30 ppm	0	0 0	0	0	0	0	0	0	0 ·	0	0	0	0	0
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OILED	0 ppm	0	0	0	0	0	0	0	0	0.	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	Õ
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	Ō	Ő	õ
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	õ	õ

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CLINICAL OBSERVATION (SUMMARY)

#### SEX : MALE

PAGE : 2

Clinical sign	Group Name	Admini	stration 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
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
DEATH	0	0	0	^	0	<u>,</u>	<u>^</u>					_	_	_	
DLA III	0 ppm		0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ORIBUND SACRIFICE	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	ů.
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
OCOMOTOR MOVEMENT DECR	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	. 0	0
	3 ppm	Ő	0	0 0	0	0	0 0	0	0	0	0	0	0	0	0
	10 ppm	õ	0 0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	õ	õ	0	0	0	0	0	0	0	0	0	0	0	0
		v	v	v	v	v	0	U	U	U	v	U	U	U	U
ATERAL	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
UNCHBACK POSITION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	õ	õ	õ	Ő	0 0	Ő
	10 ppm	0	0	Ó	0	0	ů 0	õ	õ	õ	0	0	Ő	0	0
	30 ppm	0	0	0	0	Ő	õ	Ő	õ	Ő	õ	0	0	0	0
ARALYTIC GAIT	0 ppm	0	0	0	0	0	0	0	•					_	_
meditio oni	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5 ppm 10 ppm	0	0	0	0		0	0	0	0	0	0	0	0	0
	10 ррт 30 ррт	0	0	0	0	0	0	0 0	0 0	0	0	0	0	0	0
		v	U	v	U	U	U	U	U	0	0	0	0	0	0
ASTING	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
OILED	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	ō	Õ	Õ	õ	0	Ő	0	0	0	0	0	0
	10 ppm	0	0	Õ	0	Õ	õ	Ő	õ	0	0	0	0	0	0
	30 ppm	0	0	0	0	Õ	õ	0	õ	0	0	0 0	0	0	0

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CLINICAL OBSERVATION (SUMMARY)

#### SEX : MALE

PAGE : 3

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
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
											<u> </u>				
DEATH	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0 .
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	Ó	0	0	ŏ	õ	ŏ	0	Ő	ő
	30 ppm	0	0	0	0	0	0	0	0	0	Ő	0	0	0	0
MORIBUND SACRIFICE	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	Ő	õ	Õ	Õ	õ	õ
	30 ppm	0	0	0	0	0	0	õ	0	õ	0	õ	0	0	0
LOCOMOTOR MOVEMENT DECR	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	Ó	0	Õ	Ō	Õ	õ	Ő	Ő	Ő
	30 ppm	0	0	0	0	0	0	0	0	Ő	0	Ő	0	0	0
LATERAL	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	Ő	Ő	Õ	ŏ	Ő
	10 ppm	0	0	0	0	0	0	Ō	õ	õ	Õ	õ	Ő	0 0	0
	30 ppm	0	0	0	0	0	0	Ő	õ	õ	õ	õ	0	0	0
HUNCHBACK POSITION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	- 0
	3 ppm	0	0	0	0	0	0	Õ	õ	ů 0	Ő	Ô	0	ŏ	0
	10 ppm	0	0	0	0	Õ	Ő	Ő	Ö	Ő	0	Ő	0	Ő	0
	30 ppm	0	0	0	0	0	0	0 0	õ	ŏ	0	õ	0 -	0	0
PARALYTIC GAIT	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	Õ	õ	Ő	õ	õ
	10 ppm	0	0	0	0	0	0	Ō	õ	Ő	Õ	Ő	Õ	õ	õ
	30 ppm	0	0	0	0	0	0	0	õ	õ	õ	ő	0	Ő	0 0
WASTING	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	Õ	0	õ	Õ	0 0	0	0	0 0	0
	10 ppm	0	0	0	Ō	0	0	Ő	Ő	Ő	Ő	0 0	0	õ	Õ
	30 ppm	0	0	0	0	0	0	Ő	0	Ő	ő	Ő	Ő	0	0
SOILED	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	Ő	õ	ő	0	õ	0	0	0
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	30 ppm	0	0	0	0	Ō	0	ů	õ	Ö	0	õ	0	0	0

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CLINICAL OBSERVATION (SUMMARY)

#### SEX : MALE

PAGE : 4

| linical sign           | Group Name       |        | istration 🛚 |        |        |        |        |      |        |      |      |        |        |      |        |
|------------------------|------------------|--------|-------------|--------|--------|--------|--------|------|--------|------|------|--------|--------|------|--------|
|                        |                  | 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   |
| ·                      |                  | 1      | 1           | 1      | 1      | 1      | 1      | 1    | 1      | 1    | 1    | 1      | 1      | 1    | 1      |
| ATH                    | 0                | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
| LAIN                   | 0 ppm            | 0<br>0 | 0           | 0      | 0<br>0 | 0      | 0<br>0 | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 3 ppm            |        | 0           | 0      | 0      | 0      | 0      | -    | 0      | 0    | -    | 0<br>0 | 0      | 0    | 0      |
|                        | 10 ppm<br>30 ppm | 0<br>0 | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0<br>0 | 0    | 0<br>0 |
|                        | 30 ppm           | 0      | 0           | U      | 0      | U      | U      | U    | Ų      | U    | 0    | 0      | U      | U    | 0      |
| ORIBUND SACRIFICE      | 0 ppm            | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 3 ppm            | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 10 ppm           | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 30 ppm           | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
| DCOMOTOR MOVEMENT DECR | 0 ppm            | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 3 ppm            | 0      | 0           | Ő      | 0      | 0      | 0      | 0    | 0<br>0 | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 10 ppm           | 0      | 0           | Ő      | 0      | 0<br>0 | ŏ      | 0    | 0      | õ    | Ő    | 0      | 0      | 0    | 0      |
|                        | 30 ppm           | 0      | 0<br>0      | ů<br>0 | Ő      | 0      | 0      | Ő    | 0<br>0 | 0    | 0    | 0      | 0      | 0    | 0<br>0 |
|                        | oo ppm           | ŭ      | Ũ           | v      | v      | v      | v      | Ŷ    | v      | v    | v    | v      | v      | v    | 5      |
| ATERAL                 | 0 ppm            | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 3 ppm            | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 10 ppm           | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 30 ppm           | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
| UNCHBACK POSITION      | 0 ppm            | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 3 ppm            | 0      | Ö           | 0      | 0      | 0      | 0      | 0    | 0      | Ō    | 0    | Ō      | 0      | Ō    | 0      |
|                        | 10 ppm           | 0      | 0           | 0      | Ō      | Ō      | 0      | 0    | õ      | õ    | 0    | õ      | 0      | Õ    | Ő      |
|                        | 30 ppm           | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
| ARALYTIC GAIT          | 0 ppm            | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 3 ppm            | • 0    | 0           | 0      | 0      | 0      | 0      | 0    | 0<br>0 | 0    | õ    | 0      | 0      | 0    | 0      |
|                        | 10 ppm           | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 30 ppm           | ů<br>0 | ő           | 0      | 0      | Ő      | 0      | 0    | õ      | õ    | õ    | õ      | 0      | 0    | Ő      |
|                        |                  |        |             |        |        |        |        |      |        | _    |      | _      |        | _    |        |
| VASTING                | 0 ppm            | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 3 ppm            | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 10 ppm           | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 30 ppm           | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
| OILED                  | 0 ppm            | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 3 ppm            | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 10 ppm           | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 30 ppm           | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    | 0      |

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CLINICAL OBSERVATION (SUMMARY)

#### SEX : MALE

PAGE : 5

|                        | Group Name       |        | stration W | reek-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 |
|                        |                  | 1      | 1          | 1        | 1      | 1      | 1        | 1      | 1        | 1        | 1      | 1    | 1    | 1      | 1    |
| EATH                   | mqq O            | 0      | 0          | 0        | 0      | 0      | <u>^</u> | â      | <u>^</u> |          | •      |      |      | _      |      |
| LAIN                   | 3 ppm            |        | 0          | -        | 0      | 0      | 0        | 0      | 0        | 0        | 0      | 1    | 1    | 1      | 1    |
|                        |                  | 0<br>0 | 0          | 1        | 1      | 1      | 1        | 1      | 1        | 1        | 1      | 1    | 1    | 1      | 2    |
|                        | 10 ppm<br>30 ppm | 0      | 0          | 0        | 0      | 0<br>0 | 0        | 0      | 0<br>0   | 0        | 0      | 0    | 0    | 0      | 0    |
|                        | oo bhu           | v      | U          | U        | U      | 0      | 0        | 0      | U        | 0        | 0      | 0    | 0    | 0      | - 1  |
| ORIBUND SACRIFICE      | 0 ppm            | 0      | 0          | 0        | 0      | 0      | 0        | 0      | 0        | 0        | 0      | 0    | 0    | 0      | 0    |
|                        | 3 ppm            | 0      | 0          | 0        | 0      | 0      | Ő        | Õ      | õ        | ŏ        | Õ      | õ    | 0    | 0<br>0 | 0    |
|                        | 10 ppm           | Ō      | Ō          | 0<br>0   | Ő      | õ      | õ        | 0      | Ő        | 0        | 0      | 0    | 0    | 0      | 0    |
|                        | 30 ppm           | 0      | 0          | õ        | õ      | ů<br>0 | 0        | õ      | Ő        | 0        | 0      | 0    | 0    | t      | 1    |
|                        | ••               |        |            |          | -      | -      | •        | Ū      | Ŭ        | Ŭ        | v      | Ū    | v    | L      | -    |
| OCOMOTOR MOVEMENT DECR | 0 ppm            | 0      | 0          | 0        | 0      | 0      | 0        | 0      | 0        | 0        | 0      | 0    | 0    | 0      | 0    |
|                        | 3 ppm            | 0      | 0          | 0        | 0      | 0      | 0        | 0      | 0        | 0        | 0      | 0    | 0    | 0      | 0    |
|                        | 10 ppm           | 0      | 0          | 0        | 0      | 0      | 0        | 0      | 0        | 0        | 0      | 0    | 0    | 0      | Ō    |
|                        | 30 ppm           | 0      | 0          | 0        | 0      | 0      | 0        | 0      | 0        | 0        | 0      | 0    | 0    | 0      | 0    |
| ATERAL                 | <u>^</u>         | •      | •          |          |        |        |          |        |          |          |        |      |      |        |      |
| AIERAL                 | 0 ppm<br>3 ppm   | 0<br>0 | 0<br>0     | 0        | 0<br>0 | 0      | 0        | 0      | 0        | 0        | 0      | 0    | 0    | 0      | 0    |
|                        | 10 ppm           | 0      | 0          | -        |        | 0      | 0        | 0      | 0        | 0        | 0      | 0    | 0    | 0      | 0    |
|                        | 30 ppm           | 0      | 0          | 0        | 0<br>0 | 0      | 0        | 0      | 0        | 0        | 0      | 0    | 0    | 0      | 0    |
|                        | 30 ppm           | U      | 0          | U        | U      | U      | U        | U      | U        | 0        | 0      | 0    | 0    | 0      | 0    |
| UNCHBACK POSITION      | 0 ppm            | 0      | 0          | 0        | 0      | 0      | 0        | 0      | 0        | 0        | 0      | 0    | 0    | 0      | 0    |
|                        | 3 ppm            | 0      | 0          | 0        | 0      | 0      | 0        | 0      | 0        | 0        | 0      | õ    | õ    | 0<br>0 | 0    |
|                        | 10 ppm           | 0      | 0          | 0        | 0      | 0      | 0        | 0      | 0        | Ō        | 0      | Ő    | õ    | ů      | õ    |
|                        | 30 ppm           | 0      | 0          | 0        | 0      | 0      | 0        | 0      | 0        | 0        | 0      | 0    | 0    | 0      | 0    |
| ARALYTIC GAIT          | 0 ppm            | 0      | 0          | 0        | 0      | 0      | 0        | 0      | ^        | <u>^</u> |        |      |      |        |      |
|                        | 3 ppm            | 0      | 0          | 0        | 0      | 0      | 0        | 0<br>0 | 0<br>0   | 0        | 0<br>0 | 0    | 0    | 0      | 0    |
|                        | 10 ppm           | 0      | 0          | 0        | 0      | 0      | 0        | 0      | 0        | 0<br>0   | 0      | 0    | 0    | 0      | 0    |
|                        | 30 ppm           | 0      | 0          | 0        | 0      | 0      | 0        | 0      | 0        | 0        | 0      | 0    | 0    | 0      | 0    |
|                        |                  | v      | v          | v        | U      | v      | U        | U      | v        | U        | V      | U    | U    | U      | 0    |
| ASTING                 | 0 ppm            | 0      | 0          | 0        | 0      | 0      | 0        | 0      | 0        | 0        | 0      | 0    | 0    | 0      | 0    |
|                        | 3 ppm            | 0      | 0          | 0        | 0      | 0      | 0        | 0      | 0        | 0        | 0      | Ő    | ů    | õ      | Ő    |
|                        | 10 ppm           | 0      | 0          | 0        | 0      | 0      | 0        | 0      | Ō        | Ō        | õ      | õ    | Õ    | Õ      | Õ    |
|                        | 30 ppm           | 0      | 0          | 0        | 0      | 0      | 0        | 0      | 0        | 0        | 0      | Ō    | 0    | õ      | 0    |
| OILED                  | 0 ppm            | 0      | 0          | 0        | 0      | 0      | ^        | ~      | ~        | ~        | ~      | ~    | ~    |        | _    |
| ~1000                  | 3 ppm            | 0      | 0          | 0        | 0      | 0      | 0<br>0   | 0      | 0        | 0        | 0      | 0    | 0    | 0      | 0    |
|                        | 10 ppm           | 0      | 0          | 0        | 0      | 0      | 0        | 0      | 0        | 0        | 0      | 0    | 0    | 0      | 0    |
|                        | 30 ppm           | 0      | 0          | 0        | 0      | 0      | 0        | 0      | 0        | 0        | 0      | 0    | 0    | 0      | 0    |

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CLINICAL OBSERVATION (SUMMARY)

#### SEX : MALE

PAGE : 6

linical sign	Group Name		stration W						<del></del>						
		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
······································		1	1	1	1	1	1	1	1	1	1	1	1	1	1
ATH	0 ppm	1	1	1	1	1	1	1	1	2	2	2	2	2	2
	3 ppm	2	2	2	2	2	2	2	3	3	3	3	3	3	3
	10 ppm	õ	õ	õ	õ	õ	õ	õ	0	õ	2	2	2	2	3
	30 ppm	1	2	2	2	3	3	3	3	3	4	4	4	4	4
DRIBUND SACRIFICE	0 ppm	0	0	0	0	0	0	0	0	0	0	1	1 -	1	1
	3 ppm	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	10 ppm	0	0	0	0	. 0	0	0	0	0	0	0	0	0	0
	30 ppm	1	1	1	1	1	1	1	1	1	2	2	3	3	4
DCOMOTOR MOVEMENT DECR	0 ppm	0	0	0	0	0	0	0	0	0	0	1	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	1	0	1	0	0
ATERAL	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
UNCHBACK POSITION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	1	0	0	0	1
PARALYTIC GAIT	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	· 0
	30 ppm	0	U	U	0	0	0	0	0	0	0	0	0	0	0
ASTING	0 ppm	0	0	0	0	0	0	0	0	0	0	1	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	- 1	1	0	0	0	0
OILED	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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CLINICAL OBSERVATION (SUMMARY)

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

SEX : MALE

PAGE : 7

| 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 |
|                        |                 | 1      | 1          | 1         | 1    | 1    | 1    | 1    | 1    | 1    | 1      | 1    | 1    | 1    | 1    |
| EATH                   | 0 ppm           | 2      | 2          | 2         | 2    | . 2  | 2    | 2    | 3    | 3    | 3      | 4    | 4    | 4    | 4    |
| CATH                   | 3 ppm           | 3      | 3          | 3         | 4    | 5    | 5    | 5    | 6    | 6    | 6      | 6    | 6    | 6    | 6    |
|                        | 10 ppm          | 3      | 3          | 3         | 3    | 3    | 3    | 3    | 3    | 3    | 3      | 4    | 4    | 4    | 4    |
|                        | 30 ppm          | 4      | 4          | 4         | 4    | 4    | 4    | 4    | 4    | 4    | 5      | 5    | 5    | 7    | 8    |
| ORIBUND SACRIFICE      | 0 ppm           | 1      | 2          | 2         | 2    | 2    | 2    | 2    | 2    | 3    | 3      | 3    | 4    | 4    | 4    |
| ONIDOND ONONITIOD      | mqq 0<br>mqq 2  | 1      | 1          | 1         | 1    | 1    | 1    | 1    | 1    | 1    | ů<br>1 | 1    | 2    | 2    | 2    |
|                        | 10 ppm          | 0      | 1          | 1         | 1    | 1    | 1    | 2    | 3    | 3    | 3      | 3    | 3    | 4    | 4    |
|                        | 30 ppm          | 4      | 4          | 4         | 5    | 7    | 7    | 8    | 8    | 8    | 9      | 9    | 9    | 9    | 11   |
| OCOMOTOR MOVEMENT DECR | 0 ppm           | 0      | 0          | 0         | 0    | 0    | 0    | 0    | 0    | 1    | 0      | 0    | 1    | 0    | 0    |
| SCOROTOR MOVEMENT DECK |                 | 0      | 0          | 0         | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 1    | 0    | 0    |
|                        | 3 ppm<br>10 ppm | 0      | 1          | 0         | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 1    | 0    |
|                        |                 | 0      | 0          | 0         | 0    | 1    | 0    | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 2    |
|                        | 30 ppm          | U      | U          | U         | U    | 1    | U    | U    | v    | v    | I      | v    | v    | v    | 6    |
| ATERAL                 | 0 ppm           | 0      | 0          | 0         | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    |
|                        | 3 ppm           | 0      | 0          | 0         | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    |
|                        | 10 ppm          | 0      | 0          | 0         | 0    | 0    | 0    | 0    | 1    | 0    | 0      | 0    | 0    | 0    | 0    |
|                        | 30 ppm          | 0      | 0          | 0         | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    |
| INCHBACK POSITION      | 0 ppm           | 0      | 0          | 0         | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    |
|                        | 3 ppm           | 0      | 0          | 0         | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 1    | 0    | 0    |
|                        | 10 ppm          | 0      | 0          | 0         | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    |
|                        | 30 ppm          | 0      | 0          | 0         | 0    | 0    | 0    | 0    | 0    | 0    | 2      | 1    | 1    | 0    | 2    |
| PARALYTIC GAIT         | 0 ppm           | 0      | 0          | 0         | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    |
|                        | 3 ppm           | 0      | 0          | 0         | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    |
|                        | 10 ppm          | 0      | 0          | 0         | 0    | 1    | 1    | 1    | 1    | · 1  | 1      | 1    | 1    | 1    | 1    |
|                        | 30 ppm          | 0      | 0          | 0         | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    |
| WASTING                | 0 ppm           | 0      | 0          | 0         | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    |
|                        | 3 ppm           | 0      | 0          | 0         | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 1    | 0    | 0    |
|                        | 10 ppm          | 0      | 0          | 0         | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 1    | 0    |
|                        | 30 ppm          | 0      | 0          | 0         | 0    | 0    | 0    | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 2    |
| SOILED                 | 0 ppm           | 0      | 0          | 0         | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    |
|                        | 3 ppm           | 0      | 0          | 0         | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    |
|                        | 10 ppm          | 0      | 1          | 0         | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    |
|                        | 30 ppm          | 0      | 0          | 0         | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    |

#### SEX : MALE

PAGE : 8

| Clinical sign           | Group Name | Admin | istration | Week-day _ |        |       |        |       | <br> |
|-------------------------|------------|-------|-----------|------------|--------|-------|--------|-------|------|
| -                       |            | 99-7  | 100-7     | 101-7      | 102-7  | 103-7 | 104-7  | <br>_ |      |
|                         |            | 1     | 1         | 1          | 1      | 1     | 1      |       |      |
|                         |            |       |           |            |        |       |        | <br>  | <br> |
| DEATH                   | ngq 0      | 4     | 4         | 5          | 6      | 6     | 6      |       |      |
| ULA III                 | 3 ppm      | 6     | 4<br>6    | 6          | 6      | 6     | 6      |       |      |
|                         | 10 ppm     | 5     | 5         | 5          | 5      | 6     | 6      |       |      |
|                         |            | 9     | 9         | 10         | 10     | 11    | 12     |       |      |
|                         | 30 ppm     | 9     | 9         | 10         | 10     | 11    | 12     |       |      |
| MORIBUND SACRIFICE      | 0 ppm      | 4     | 4         | 4          | 4      | 4     | 4      |       |      |
|                         | 3 ppm      | 2     | 2         | 2          | 2      | 2     | 2      |       |      |
|                         | 10 ppm     | 4     | 4         | 5          | 6      | 6     | 6      |       |      |
|                         | 30 ppm     | 13    | 13        | 14         | 15     | 15    | 15     |       |      |
| LOCONOTOR MOVEMENT DECR | 0 ppm      | 0     | 0         | 0          | 0      | 0     | 0      |       |      |
|                         | 3 ppm      | 0     | ů<br>0    | Õ          | Õ      | Õ     | Ő      |       |      |
|                         | 10 ppm     | Õ     | Õ         | 1          | ů      | Ő     | õ      |       |      |
|                         | 30 ppm     | 0     | 0         | 1          | 1      | 0     | 0      |       |      |
|                         |            |       |           |            | -      |       |        |       |      |
| LATERAL                 | 0 ppm      | 0     | 0         | 0          | 0      | 0     | 0      |       |      |
|                         | 3 ppm      | 0     | 0         | 0          | 0      | 0     | 0      |       |      |
|                         | 10 ppm     | 0     | 0         | 0          | 0      | 0     | 0      |       |      |
|                         | 30 ppm     | 0     | 0         | 0          | 0      | 0     | 0      |       |      |
| HUNCHBACK POSITION      | 0 ppm      | 0     | 0         | 0          | 0      | 0     | 0      |       |      |
|                         | 3 ppm      | Ő     | 0<br>0    | Ő          | õ      | 0     | Ő      |       |      |
|                         | 10 ppm     | o     | ů         | 0          | 0      | 0     | ů<br>0 |       |      |
|                         | 30 ppm     | 2     | 2         | 2          | 3      | 2     | 5      |       |      |
|                         | oo ppu     | 5     | 2         | 2          | v      | 2     | v      |       |      |
| PARALYTIC GAIT          | 0 ppm      | 0     | 0         | 1          | 0      | 0     | 1      |       |      |
|                         | 3 ppm      | 0     | 0         | 0          | 0      | 0     | 0      |       |      |
|                         | 10 ppm     | 0     | 0         | 0          | 0      | 0     | 0      |       |      |
|                         | 30 ppm     | 0     | 0         | 0          | 0      | 0     | 0      |       |      |
| WASTING                 | 0 ppm      | 0     | 0         | 0          | 0      | 0     | 0      |       |      |
|                         | 3 ppm      | õ     | Ő         | ů<br>0     | 0<br>0 | 0     | ů<br>0 |       |      |
|                         | 10 ppm     | ů     | 0<br>0    | Õ          | ŏ      | Ő     | 0      |       |      |
|                         | 30 ppm     | 0     | 0<br>0    | Ő          | 1      | 0     | 0<br>0 |       |      |
|                         |            |       | -         | 5          | •      | 2     | -      |       |      |
| SOILED                  | 0 ppm      | 0     | 0         | 1          | 0      | 0     | 0      |       |      |
|                         | 3 ppm      | 0     | 0         | 0          | 0      | 0     | 0      |       |      |
|                         | 10 ppm     | 0     | 0         | 0          | 0      | 0     | 0      |       |      |
|                         | 30 ppm     | 0     | 0         | 0          | 0      | 0     | 0      |       |      |
|                         |            |       |           |            |        |       |        |       |      |

CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

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#### SEX : MALE

PAGE : 9

| Clinical sign            | Group Name | Admini | stration We |     |     |     |     |          |     |     |      |      |        |          |      |
|--------------------------|------------|--------|-------------|-----|-----|-----|-----|----------|-----|-----|------|------|--------|----------|------|
|                          |            | 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 |
|                          |            | 1      | 1           | 1   | 1   | 1   | 1   | 1        | 1   | 1   | 1    | 1    | 1      |          | 1    |
|                          |            | 0      |             |     | •   |     | •   | <u>^</u> | 2   |     |      | 0    |        | <u>^</u> | •    |
| PILOERECTION             | mqq 0      | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 3 ppm      | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 10 ppm     | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 30 ppm     | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
| FROG BELLY               | 0 ppm      | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 3 ppm      | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 10 ppm     | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 30 ppm     | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | . 0      | 0    |
| SOILED PERI GENITALIA    | 0 ppm      | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 3 ppm      | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 10 ppm     | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 30 ppm     | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
| XOPHTHALMOS              | 0 ppm      | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 3 ppm      | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 10 ppm     | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 1    | 1    | 1      | 1        | 1    |
|                          | 30 ppm     | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 1    | 1    | 1      | 1        | 1    |
| EYE OPACITY              | 0 ppm      | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 3 ppm      | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 10 ppm     | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 30 ppm     | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
| CATARACT                 | 0 ppm      | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 3 ppm      | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 10 ppm     | Ő      | ů           | õ   | õ   | 0   | 0   | Õ        | õ   | õ   | õ    | õ    | 0<br>0 | Ő        | 0    |
|                          | 30 ppm     | õ      | 0           | õ   | 0   | õ   | 0   | 0        | õ   | o   | õ    | 0    | 0      | 0        | Ő    |
| CORNEAL OPACITY          | 0 ppm      | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 3 ppm      | 0      | Ō           | 0   | Ō   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 10 ppm     | Ō      | Õ           | Õ   | Õ   | Õ   | Õ   | Õ        | Õ   | Õ   | Õ    | 0    | 0      | Õ        | 0    |
|                          | 30 ppm     | õ      | õ           | õ   | Ő   | 0   | õ   | 0        | 0   | Ő   | 0    | õ    | Ő      | õ        | 0    |
| ABNORMAL GROWTH OF TEETH | mqq 0      | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 3 ppm      | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 10 ppm     | 0      | 0           | 0   | 0   | 0   | 0   | 0        | 0   | 0   | 0    | 0    | 0      | 0        | 0    |
|                          | 30 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 : MALE

PAGE : 10

| Clinical sign                    | Group Name    | Admini | stration W | leek-dav |        |        |      |        |        |        |        |      |      |        |        |
|----------------------------------|---------------|--------|------------|----------|--------|--------|------|--------|--------|--------|--------|------|------|--------|--------|
|                                  | of oup Induio | 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   |
|                                  |               | 1      | 1          | 1        | 1      | 1      | 1    | 1      | 1      | 1      | 1      | 1    | 1    | 1      | 1      |
|                                  |               |        |            |          |        |        |      |        |        |        |        | -    |      |        |        |
| PILOERECTION                     | 0 ppm         | 0      | 0          | 0        | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
|                                  | 3 ppm         | 0      | 0          | 0        | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
|                                  | 10 ppm        | 0      | 0          | 0        | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
|                                  | 30 ppm        | 0      | 0          | 0        | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
| ROG BELLY                        | 0 ppm         | 0      | 0          | 0        | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
|                                  | 3 ppm         | 0      | 0          | 0        | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
|                                  | 10 ppm        | 0      | 0          | 0        | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
|                                  | 30 ppm        | 0      | 0          | 0        | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
| SOILED PERI GENITALIA            | 0 ppm         | 0      | 0          | 0        | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
|                                  | 3 ppm         | 0      | 0          | 0        | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
|                                  | 10 ppm        | 0      | 0          | 0        | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
|                                  | 30 ppm        | 0      | 0          | 0        | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
| EXOPHTHALMOS                     | 0 ppm         | 0      | 0          | 0        | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
|                                  | 3 ppm         | 0      | 0          | 0        | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
|                                  | 10 ppm        | 1      | 1          | 1        | 1      | 1      | 1    | 1      | · 1    | 1      | 1      | 1    | 1    | 1      | 1      |
|                                  | 30 ppm        | 1      | 1          | 1        | 1      | 1      | 1    | 1      | 1      | 1      | 1      | 1    | 1    | 1      | 1      |
| EYE OPACITY                      | 0 ppm         | 0      | 0          | 0        | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
|                                  | 3 ppm         | Õ      | õ          | ů<br>0   | õ      | õ      | õ    | Ő      | õ      | 0      | 0<br>0 | Ő    | Õ    | Õ      | 0      |
|                                  | 10 ppm        | õ      | õ          | ů        | Õ      | õ      | õ    | Ő      | õ      | õ      | ů<br>0 | Ő    | 0    | 0      | Ō      |
|                                  | 30 ppm        | 0      | 0          | 0        | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
| CATARACT                         | 0 ppm         | 0      | 0          | 0        | 0      | 0      | 0    | 0      | 0      | 0      | 1      | 1    | 1    | 1      | 1      |
|                                  | 3 ppm         | õ      | ů          | 0        | 0<br>0 | 0<br>0 | Ő    | Ő      | õ      | 0<br>0 | 0      | Ô    | Ô    | Ō      | Ō      |
|                                  | 10 ppm        | õ      | Ő          | 0        | 0      | 1      | 1    | 1      | 1      | 1      | 1      | 1    | 1    | 1      | 1      |
|                                  | 30 ppm        | 0      | 0          | 0        | 0      | ō      | 0    | 0      | 1      | 1      | 1      | 1    | 1    | 1      | 1      |
| CORNEAL OPACITY                  | 0 ppm         | 0      | 0          | 0        | 0      | 0      | . 0  | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
| condition of the state           | 3 ppm         | 0      | 0          | 0        | 0      | 0      | 0    | 0      | 0      | õ      | õ      | 0    | Ő    | 0      | õ      |
|                                  | 10 ppm        | õ      | 0<br>0     | õ        | Ő      | 0<br>0 | õ    | 0<br>0 | 0      | õ      | õ      | Õ    | Ő    | õ      | ŏ      |
|                                  | 30 ppm        | Ő      | Ő          | õ        | Õ      | Õ      | Õ    | 0      | õ      | õ      | õ      | 0    | 0    | 0      | 0      |
| ABNORMAL GROWTH OF TEETH         | 0 ppm         | 0      | 0          | 0        | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
| The offering offering of The III | 3 ppm         | 0      | 0          | ŏ        | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0      | ő      |
|                                  | 10 ppm        | 0      | õ          | Ő        | 0      | 0      | 0    | 0      | 0<br>0 | Ő      | Ő      | Ő    | 0    | 0      | ů<br>0 |
|                                  | 30 ppm        | Ő      | 0          | ů        | Õ      | 0<br>0 | Ő    | Ő      | õ      | 0      | Ő      | õ    | 0    | 0<br>0 | 0<br>0 |

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CLINICAL OBSERVATION (SUMMARY)

### SEX : MALE

PAGE : 11

| linical sign             | Group Name | Admini | stration N | /eek-day |          |          |      |          |      |      |      |      |      |      |      |
|--------------------------|------------|--------|------------|----------|----------|----------|------|----------|------|------|------|------|------|------|------|
|                          |            | 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 |
|                          |            | 1      | 1          | 1        | 1        | 1        | 1    | 1        | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| LOFFECTION               | 0          |        | 0          |          | <u>^</u> | <u>^</u> | 0    | <u>^</u> | 0    | •    | 0    | 0    | 0    | 0    | 0    |
| TLOERECTION              | 0 ppm      | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 3 ppm      | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ROG BELLY                | 0 ppm      | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 3 ppm      | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| OILED PERI GENITALIA     | 0 ppm      | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 3 ppm      | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | . 0  |
|                          | 10 ppm     | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| XOPHTHALMOS              | 0 ppm      | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 3 ppm      | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 1      | 1          | 1        | 1        | 1        | 1    | 1        | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                          | 30 ppm     | 1      | 1          | 1        | 1        | 1        | 1    | 1        | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| YE OPACITY               | 0 ppm      | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 3 ppm      | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | . 0  |
|                          | 30 ppm     | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT                 | 0 ppm      | 1      | 1          | 1        | 1        | 1        | 1    | 1        | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                          | 3 ppm      | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 1      | 1          | 1        | , 1      | 1        | 1    | 1        | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                          | 30 ppm     | 1      | 1          | 1        | 1        | 1        | 1    | 1        | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| CORNEAL OPACITY          | 0 ppm      | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 3 ppm      | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL GROWTH OF TEETH | 0 ppm      | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 3 ppm      | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0      | 0          | 0        | 0        | 0        | 0    | 0        | 0    | 0 '  | 0    | 0    | 0    | 0    | 0    |

CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

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#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

#### SEX : MALE

PAGE : 12

| 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   |
|                          |            | 1      | 1           | 1       | 1    | 1      | 1    | 1      | 1    | 1    | 1    | 1    | 1      | 1      | 1      |
|                          |            |        |             |         |      |        |      |        |      |      |      |      |        |        |        |
| PILOERECTION             | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      |
|                          | 3 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      |
|                          | 10 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      |
|                          | 30 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      |
| ROG BELLY                | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      |
|                          | 3 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      |
|                          | 10 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      |
|                          | 30 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      |
| SOILED PERI GENITALIA    | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      |
|                          | 3 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      |
|                          | 10 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      |
|                          | 30 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      |
| EXOPHTHALMOS             | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      |
|                          | 3 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      |
|                          | 10 ppm     | 1      | 1           | 1       | 1    | 1      | 1    | 1      | 1    | 1    | 1    | 1    | 1      | 1      | 1      |
|                          | 30 ppm     | 1      | 1           | 1       | 1    | 1      | 1    | ĩ      | 1    | ĩ    | 1    | 1    | 1      | 1      | ĩ      |
| EYE OPACITY              | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      |
|                          | 3 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0    | Ō    | 0    | 0    | 0      | 0      | 0      |
|                          | 10 ppm     | 0      | 0           | 0       | Ő    | 0      | õ    | ů      | ů    | 0    | õ    | õ    | Õ      | 0      | õ      |
|                          | 30 ppm     | 0      | 0           | Ő       | Õ    | ů<br>0 | 0    | ů<br>0 | Ő    | 0    | 0    | Ő    | ů      | ů<br>0 | 0      |
| CATARACT                 | 0 ppm      | 1      | 1           | 1       | 1    | 1      | 1    | 1      | 1    | 2    | 2    | 2    | 2      | 2      | 2      |
| ···· •                   | 3 ppm      | Ô      | 0           | 0       | Ô    | 0      | 0    | 0      | 0    | õ    | 0    | õ    | Ő      | 0      | õ      |
|                          | 10 ppm     | 1      | 1           | 1       | 1    | 1      | 1    | 1      | 1    | 1    | ĩ    | ĩ    | ı<br>1 | 1      | 1      |
|                          | 30 ppm     | 1      | 1           | 1       | 1    | 1      | 1    | 1      | 1    | 1    | 1    | 1    | 1      | 1      | 1      |
| CORNEAL OPACITY          | mqq 0      | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      |
|                          | 3 ppm      | 0      | Ő           | 0       | 0    | 0      | 0    | 0      | õ    | ŏ    | 0    | 0    | Ő      | 0      | 0      |
|                          | 10 ppm     | 0      | 0           | õ       | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      |
|                          | 30 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      |
| ABNORMAL GROWTH OF TEETH | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      |
|                          | 3 ppm      | 0      | õ           | 0       | Ő    | 0      | 0    | 0      | õ    | 0    | 0    | 0    | 0      | 0      | 0      |
|                          | 10 ppm     | 0      | Ő           | Ő       | 0    | 0      | ŏ    | 0      | 0    | 0    | 0    | Ő    | 0      | 0      | 0      |
|                          | 30 ppm     | 0<br>0 | õ           | Ő       | õ    | 0      | 0    | 0      | 0    | 0    | õ    | 0    | 0      | 0      | ů<br>0 |
|                          | oo ppm     |        | v           |         | v    | 5      | v    | v      | 0    | v    | v    | v    | v      | v      | 0      |

#### SEX : MALE

PAGE : 13

| Clinical sign           | Group Name | Admini | istration 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   |
|                         |            | 1      | 1           | 1       | 1    | 1    | 1    | 1      | 1    | 1      | 1      | 1      | 1             | 1      | 1      |
|                         |            |        |             |         |      |      |      |        |      |        |        |        |               |        |        |
| PILOERECTION            | 0 ppm      | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | 0      | 0      |
|                         | 3 ppm      | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | 0      | 0      |
|                         | 10 ppm     | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | 0      | 0      |
|                         | 30 ppm     | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | 0      | 0      |
| ROG BELLY               | 0 ppm      | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | . 0    | 0      |
|                         | 3 ppm      | 0      | 0           | 0       | Ő    | õ    | õ    | õ      | õ    | õ      | 0      | 0      | 0             | 0      | 0      |
|                         | 10 ppm     | 0<br>0 | õ           | õ       | 0    | 0    | ŏ    | 0      | 0    | 0      | 0      | 0      | 0             | 0      | 0      |
|                         | 30 ppm     | Õ      | Ő           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | -      |        |
|                         | oo ppin    | , v    | v           | v       | v    | U    | v    | U      | U    | U      | U      | U      | U             | 0      | 0      |
| SOILED PERI GENITALIA   | 0 ppm      | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | 0      | 0      |
|                         | 3 ppm      | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | 0      | 0      |
|                         | 10 ppm     | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | 0      | 0      |
|                         | 30 ppm     | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 1             | 0      | 0      |
| XOPHTHALMOS             | 0 ppm      | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | 0      | 0      |
|                         | 3 ppm      | 0      | 0           | 0       | Õ    | õ    | õ    | õ.     | õ    | ŏ      | 0      | 0<br>0 | 0             | 0      | 0      |
|                         | 10 ppm     | 1      | 1           | 1       | 1    | 1    | 1    | 1      | 1    | 1      | 1      | 1      |               |        |        |
|                         | 30 ppm     | 1      | 1           | 1       | 1    | 1    | 1    | 1      | 1    | 1      | 1      | 1      | 1<br>1        | 1<br>1 | 1<br>1 |
|                         |            |        |             |         |      |      |      |        | -    | -      | •      | •      | 1             | 1      | 1      |
| EYE OPACITY             | 0 ppm      | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | 0      | 0      |
|                         | 3 ppm      | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | 0      | 0      |
|                         | 10 ppm     | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | 0      | 0      |
|                         | 30 ppm     | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | 0      | 0      |
| CATARACT                | 0 ppm      | 3      | 3           | 3       | 3    | 3    | 3    | 3      | 3    | 3      | 3      | 3      | 0             | 0      |        |
| -                       | 3 ppm      | 0      | 0           | õ       | 0    | 0    | 0    | 0      | 0    | 0      | 3<br>0 | 3<br>0 | 3             | 3      | 3      |
|                         | 10 ppm     | 1      | 1           | 1       | 1    | 1    | 1    | 1      | 1    |        | -      |        | 0             | 0      | 0      |
|                         | 30 ppm     | 1      | 1           | 1       | 1    | 1    | 1    | 1<br>2 | 1    | 1<br>2 | 1<br>2 | 1<br>2 | $\frac{1}{2}$ | 1<br>2 | 1<br>2 |
| CODNEAL ODACITY         | -          |        | -           |         |      |      |      |        |      |        |        |        | 5             | 5      | ÷      |
| CORNEAL OPACITY         | 0 ppm      | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | 0      | 0      |
|                         | 3 ppm      | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | 0      | 0      |
|                         | 10 ppm     | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | 0      | 0      |
|                         | 30 ppm     | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | 0      | 0      |
| BNORMAL GROWTH OF TEETH | 0 ppm      | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | 0      | 0      |
|                         | 3 ppm      | Õ      | Õ           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | 0      | 0      |
|                         | 10 ppm     | Ő      | õ           | 0       | õ    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | 0      |        |
|                         | 30 ppm     | ŏ      | õ           | Ő       | õ    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0             | 0      | 0      |

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CLINICAL OBSERVATION (SUMMARY)

#### SEX : MALE

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PAGE: 14

| Clinical sign            | Group Name | Admini | istration W |      |      |          |          |      |      |      |      |        |        |      |      |
|--------------------------|------------|--------|-------------|------|------|----------|----------|------|------|------|------|--------|--------|------|------|
|                          |            | 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 |
|                          |            | 1      | 1           | 1    | 1    | 1        | 1        | 1    | 1    | 1    | 1    | 1      | 1      | 1    | 1    |
| PILOERECTION             | 0          | 0      | 0           | 0    | 0    | <u>,</u> | <u>^</u> |      |      |      |      |        |        | _    | _    |
| LOERECTION               | 0 ppm      | 0      | 0           | 0    | 0    | 0        | 0        | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    |
|                          | 3 ppm      | 0      | 0           | 0    | 0    | 0        | 0        | 0    | . 0  | 0    | 0    | 0      | 0      | 0    | 0    |
|                          | 10 ppm     | 0      | 0           | 0    | 0    | 0        | 0        | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    |
|                          | 30 ppm     | 0      | 0           | 0    | 0    | 0        | 0        | 0    | 0    | 0    | 1    | 0      | 0      | 0    | 0    |
| ROG BELLY                | 0 ppm      | 0      | 0           | 0    | 0    | 0        | 0        | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    |
|                          | 3 ppm      | 0      | 0           | 0    | 0    | 0        | 0        | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    |
|                          | 10 ppm     | 0      | 0           | 0    | 0    | 0        | 0        | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 1    |
|                          | 30 ppm     | 0      | 1           | 1    | 1    | 0        | 0        | 1    | 1    | 2    | 2    | 2      | 2      | 1    | 1    |
| OILED PERI GENITALIA     | 0 ppm      | 0      | 0           | 0    | 0    | 0        | 0        | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    |
|                          | 3 ppm      | 0      | 0           | 0    | 0    | 0        | 0        | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    |
|                          | 10 ppm     | 0      | 0           | 0    | 0    | 0        | 0        | 0    | 0    | 0    | 0    | 0      | 0      | Ó    | 0    |
|                          | 30 ppm     | 0      | 0           | 0    | 0    | 0        | 0        | 0    | 0    | 0    | 1    | 0      | 0      | 0    | 0    |
| XOPHTHALMOS              | 0 ppm      | 0      | 0           | 0    | 0    | 0        | 0        | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    |
|                          | 3 ppm      | 0      | 0           | 0    | 0    | 0        | 0        | 0    | 0    | 0    | 0    | 0      | 0      | Ō    | Ō    |
|                          | 10 ppm     | 1      | 1           | 1    | 0    | 0        | 0        | 0    | 0    | Ō    | 0    | 0      | Ő      | 0    | Ō    |
|                          | 30 ppm     | 1      | 1           | 1    | 0    | 0        | 0        | 0    | 0    | 0    | 0    | õ      | 0      | 0    | ů    |
| YE OPACITY               | mqq 0      | 0      | 0           | 0    | 0    | 0        | 0        | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    |
|                          | 3 ppm      | 0      | 0           | 0    | 0    | 0        | Ő        | Õ    | õ    | õ    | õ    | 0      | Ő      | 0    | õ    |
|                          | 10 ppm     | 0      | 0           | 0    | Ő    | Õ        | õ        | 0    | õ    | õ    | 0    | 0<br>0 | 0      | Ő    | 0    |
|                          | 30 ppm     | 0      | 0           | 0    | 0    | Ő        | Ő        | 0    | 0    | Ő    | Ő    | Ő      | 0<br>0 | 0    | 0    |
| CATARACT                 | 0 ppm      | 3      | 3           | 3    | 3    | 3        | 3        | 3    | 3    | 3    | 3    | 3      | 3      | 3    | 3    |
|                          | 3 ppm      | Ő      | Õ           | Õ    | õ    | õ        | õ        | õ    | õ    | 0    | õ    | 0      | 0      | 0    | 0    |
|                          | 10 ppm     | ĩ      | 1           | 1    | 1    | 1        | 1        | 1    | 1    | 1    | 1    | 1      | 1      | 1    | 1    |
|                          | 30 ppm     | 2      | 2           | 2    | 2    | 2        | 2        | 2    | 2    | 2    | 2    | 1<br>2 | 1<br>2 | 3    | 3    |
| CORNEAL OPACITY          | 0 ppm      | 0      | 0           | 0    | 0    | 0        | 0        | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    |
|                          | 3 ppm      | õ      | õ           | õ    | õ    | 0        | 0        | õ    | 0    | 0    | 0    | 0      | 0      | 0    | 0    |
|                          | 10 ppm     | õ      | ŏ           | 0    | ŏ    | 0        | 0        | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    |
|                          | 30 ppm     | 0      | 0           | õ    | 0    | õ        | 0        | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    |
| ABNORMAL GROWTH OF TEETH | 0 ppm      | 0      | 0           | 0    | 0    | 0        | 0        | 0    | 0    | 0    | 0    | 0      | D      | 0    | 0    |
|                          | 3 ppm      | õ      | Ő           | õ    | õ    | 0<br>0   | Ő        | Ő    | 0    | 0    | 0    | 0      | 0      | 0    | 0    |
|                          | 10 ppm     | õ      | Ő           | 0    | 0    | ŏ        | 0        | 0    | 0    | 0    | 0    | 0      | 0      | 0    |      |
|                          | 30 ppm     | 0      | õ           | 0    | 0    | 0        | 0        | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    |
|                          | an hhu     | U      | v           | 0    | U    | 0        | U        | Ų    | U    | U    | Ų    | U      | U      | U    | 0    |

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CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

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#### SEX : MALE

PAGE : 15

| 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 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
|                          |            | 1      | 1          | 1        | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1.   | 1    |
|                          |            |        |            |          |      |      |      |      |      |      |      |      |      |      |      |
| ILOERECTION              | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    |
|                          | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    |
| ROG BELLY                | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 3 ppm      | 0      | 1          | 1        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 1      | 1          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0      | 1          | 1        | 1    | 2    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| OILED PERI GENITALIA     | 0 ppm      | 1      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    |
|                          | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0      | 0          | 0        | 0    | 1    | 1    | 1    | 2    | 1    | 1    | 1    | 1    | 1    | 1    |
|                          | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| XOPHTHALMOS              | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0      | 0          | 0        | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
| YE OPACITY               | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 0    | 0    |
|                          | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ATARACT                  | 0 ppm      | 3      | 3          | 3        | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |
|                          | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 1      | 1          | 1        | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                          | 30 ppm     | 3      | 3          | 3        | 3    | 3    | 2    | 2    | 2    | 1    | 1    | 1    | 1    | 1    | 1    |
| CORNEAL OPACITY          | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
| ABNORMAL GROWTH OF TEETH | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    |
|                          | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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CLINICAL OBSERVATION (SUMMARY)

#### SEX : MALE

PAGE : 16

| Clinical sign                  | Group Name |        | istration N | Week-day _ |       |       |       |
|--------------------------------|------------|--------|-------------|------------|-------|-------|-------|
|                                |            | 99-7   | 100-7       | 101-7      | 102-7 | 103-7 | 104-7 |
|                                |            | 1      | 1           | 1          | 1     | 1     | 1     |
|                                |            |        |             |            |       |       |       |
| PILOERECTION                   | 0          | 0      | 0           | 0          | 0     | 0     | 0     |
| FILUERECTION                   | 0 ppm      | 0      | 0           | 0          |       |       |       |
|                                | 3 ppm      | 0      | 0           | 0          | 0     | 0     | 0     |
|                                | 10 ppm     | 0      | 0           | 0          | 0     | 0     | 0     |
|                                | 30 ppm     | 0      | 0           | 0          | 1     | 0     | 1     |
| FROG BELLY                     | 0 ppm      | 0      | 0           | 0          | 0     | 0     | 0     |
|                                | 3 ppm      | 0      | 0           | 0          | 0     | 0     | 0     |
|                                | 10 ppm     | 0      | 0           | 0          | 0     | 0     | 0     |
|                                | 30 ppm     | 0      | 1           | 1          | 0     | 0     | 0     |
| SOILED PERI GENITALIA          | 0 ppm      | 0      | 0           | 1          | 0     | 0     | 0     |
|                                | 3 ppm      | 0      | 0           | 0          | 0     | 0     | 0     |
|                                | 10 ppm     | õ      | õ           | Õ          | õ     | õ     | Ő     |
|                                | 30 ppm     | ů<br>0 | ů<br>0      | Ő          | 0     | Õ     | Ő     |
|                                | oo ppu     | 5      | v           | v          |       | Ť     | Ť     |
| EXOPHTHALMOS                   | 0 ppm      | 0      | 0           | 0          | 0     | 0     | 0     |
|                                | 3 ppm      | 0      | 0           | 0          | 0     | 0     | 0     |
|                                | 10 ppm     | 0      | 0           | 0          | 0     | 0     | 0     |
|                                | 30 ppm     | 0      | 0           | 0          | 0     | 0     | 0     |
| EYE OPACITY                    | 0 ppm      | 0      | 0           | 0          | 0     | 0     | 0     |
|                                | 3 ppm      | 0      | 0           | 0          | 0     | 0     | 0     |
|                                | 10 ppm     | õ      | Õ           | Ő          | õ     | õ     | Ő     |
|                                | 30 ppm     | Ő      | Õ           | Õ          | 0     | 0     | 1     |
|                                |            |        |             |            |       |       |       |
| CATARACT                       | 0 ppm      | 3      | 3           | 3          | 3     | 3     | 3     |
|                                | 3 ppm      | 0      | 0           | 0          | 0     | 0     | 0     |
|                                | 10 ppm     | 1      | 1           | 1          | 1     | 1     | 1     |
|                                | 30 ppm     | 0      | 0           | 0          | 0     | 0     | 0     |
| CORNEAL OPACITY                | 0 ppm      | 0      | 0           | 0          | 0     | 0     | 0     |
| · · · · · ·                    | 3 ppm      | 0      | 0           | 0          | 0     | 0     | 0     |
|                                | 10 ppm     | 0      | 0           | 0          | 0     | 0     | 0     |
|                                | 30 ppm     | 0      | 0           | 0          | 0     | 0     | 0     |
| ABNORMAL GROWTH OF TEETH       | 0 ppm      | 0      | 0           | 0          | 0     | 0     | 0     |
| Lassing the state of the state | 3 ppm      | 0      | 0           | 0          | 0     | 0     | 0     |
|                                | 10 ppm     | 0      | 0           | Ő          | 0     | 0     | õ     |
|                                | 30 ppm     | ŏ      | 0           | 0<br>0     | õ     | õ     | ů     |
|                                | oo ppu     | v      | v           | •          | v     | Ū.    | v     |

CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

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#### SEX : MALE

PAGE : 17

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| 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   |
|               |            | 1      | 1           | 1      | 1   | 1   | 1   | 1      | 1      | 1      | 1      | 1    | 1    | 1      | 1      |
|               |            |        |             |        |     |     |     |        |        |        |        |      |      |        |        |
| NTERNAL MASS  | mqq 0      | 0      | 0           | 0      | 0   | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
|               | 3 ppm      | 0      | 0           | 0      | 0   | 0   | 0   | 0      | 0      | 0      | 0      | 0    | Õ    | õ      | ů      |
|               | 10 ppm     | 0      | 0           | 0      | 0   | 0   | 0   | 0      | Ō      | Õ      | Ő      | Õ    | õ    | õ      | 0      |
|               | 30 ppm     | 0      | 0           | 0      | 0   | 0   | 0   | 0      | 0      | 0      | õ      | 0    | 0    | 0      | Õ      |
| NOSE          | 0 ppm      | 0      | 0           | 0      | 0   | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
|               | 3 ppm      | 0      | 0           | 0      | 0   | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    | 0      | Ō      |
|               | 10 ppm     | 0      | 0           | 0      | 0   | 0   | 0   | 0      | 0      | 0      | Ő      | Õ    | 0    | 0      | õ      |
|               | 30 ppm     | 0      | 0           | 0      | 0   | 0   | 0   | 0      | Ő      | ő      | õ      | 0    | 0    | 0      | 0      |
| . EYE         | 0 ppm      | 0      | 0           | 0      | 0   | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
|               | 3 ppm      | 0      | 0           | 0      | 0   | 0   | 0   | 0      | 0      | Ó      | 0      | Ō    | 0    | Ō      | 0      |
|               | 10 ppm     | 0      | 0           | 0      | 0   | Ō   | 0   | Ō      | Õ      | õ      | õ      | õ    | Ő    | Ö      | 0      |
|               | 30 ppm     | 0      | 0           | 0      | 0   | 0   | 0   | 0      | 0      | 0<br>0 | õ      | Ő    | 0    | 0      | 0      |
| .PERI MOUTH   | 0 ppm      | 0      | 0           | 0      | 0   | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
|               | 3 ppm      | 0      | 0           | 0      | 0   | Õ   | õ   | õ      | Õ      | õ      | 0      | 0    | 0    | 0      | 0      |
|               | 10 ppm     | 0      | 0           | 0      | 0   | Ő   | õ   | 0      | 0<br>0 | 0      | 0      | 0    | 0    | 0      |        |
|               | 30 ppm     | Ő      | õ           | 0      | 0   | Ő   | ő   | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0<br>0 |
| ORAL CAVITY   | 0 ppm      | 0      | 0           | 0      | 0   | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
|               | 3 ppm      | 0      | 0           | 0      | 0   | 0   | õ   | Õ      | õ      | Õ      | 0<br>0 | 0    | 0    | Õ      | 0      |
|               | 10 ppm     | 0      | 0           | õ      | Õ   | õ   | õ   | 0<br>0 | Ő      | 0<br>0 | ŏ      | 0    | 0    | 0      | 0      |
|               | 30 ppm     | 0      | 0           | 0      | õ   | 0   | õ   | 0<br>0 | 0      | õ      | 0      | 0    | 0    | 0      | 0      |
| . MANDIBULAR  | 0 ppm      | 0      | 0           | 0      | 0   | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
|               | 3 ppm      | 0      | 0           | 0      | 0   | 0   | 0   | 0      | Ō      | Ő      | õ      | õ    | õ    | 0<br>0 | 0      |
|               | 10 ppm     | 0      | 0           | 0      | 0   | 0   | 0   | Õ      | õ      | ŏ      | õ      | Ő    | 0    | 0      | 0      |
|               | 30 ppm     | 0      | 0           | Ő      | õ   | ō   | 0   | 0      | õ      | 0      | 0      | 0    | 0    | 0      | 0      |
| I. EAR        | 0 ppm      | 0      | 0           | 0      | 0   | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
|               | 3 mag      | 0      | 0           | 0      | 0   | 0   | õ   | õ      | õ      | Õ      | Ő      | Ő    | Ő    | õ      | 0      |
|               | 10 ppm     | 0      | Ō           | Õ      | õ   | õ   | õ   | Ő      | Ő      | õ      | 0      | Ő    | 0    | 0      | 0      |
|               | 30 ppm     | 0      | 0           | Ő      | õ   | Ő   | ŏ   | 0      | 0      | 0<br>0 | 0      | 0    | 0    | 0      | 0      |
| . PERI EAR    | 0 ppm      | 0      | 0           | 0      | 0   | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      |
|               | 3 ppm      | 0      | 0           | 0      | 0   | 0   | 0   | 0      | Ō      | õ      | 0      | õ    | 0    | õ      | 0      |
|               | 10 ppm     | 0      | 0           | 0      | 0   | 0   | 0   | Ő      | õ      | Ő      | 0      | õ    | 0    | 0      | 0      |
|               | 30 ppm     | 0      | 0           | 0      | 0   | 0   | 0   | Ő      | õ      | ő      | 0      | õ    | 0    | ŏ      | õ      |

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CLINICAL OBSERVATION (SUMMARY)

#### SEX : MALE

PAGE : 18

| 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     |
|               |            | 1      | 1           | 1        | 1    | 1      | 1      | 1        | 1      | 1      | 1    | 1    | 1      | 1    | 1        |
|               |            |        |             |          |      |        |        |          |        |        |      |      |        |      |          |
| NTERNAL MASS  | 0 ppm      | 0      | 0           | 0        | 0    | 0      | 0      | 0        | 0      | 0      | 0    | 0    | 0      | 0    | 0        |
|               | 3 ppm      | 0      | 0           | 0        | 0    | 0      | 0      | 0        | 0      | 0      | 0    | 0    | 0      | 0    | 0        |
|               | 10 ppm     | 0      | 0           | 0        | 0    | 0      | 0      | 0        | 0      | 0      | 0    | 0    | 0      | 0    | 0        |
|               | 30 ppm     | 0      | 0           | 0        | 0    | 0      | 0      | 0        | 0      | 0      | 0    | 0    | 0      | 0    | 0        |
| . NOSE        | 0 ppm      | 0      | 0           | 0        | 0    | 0      | 0      | 0        | 0      | 0      | 0    | 0    | 0      | 0    | 0        |
|               | 3 ppm      | 0      | 0           | 0        | 0    | 0      | 0      | 0        | 0      | 0      | 0    | õ    | Õ      | õ    | õ        |
|               | 10 ppm     | 0      | 0           | 0        | 0    | 0      | Ő      | Ő        | 0      | õ      | 0    | Ő    | 0      | 0    | 0        |
|               | 30 ppm     | 0      | 0           | 0        | 0    | 0<br>0 | ů<br>0 | 0        | 0      | 0      | 0    | 0    | 0      | 0    | 0        |
| I. EYE        | 0 ppm      | 0      | 0           | 0        | 0    | 0      | 0      | 0        | 0      | 0      | 0    | 0    | 0      | 0    | ~        |
|               | 3 ppm      | 0      | Õ           | 0<br>0   | 0    | 0<br>0 | 0      | 0        | 0      | 0      | 0    | 0    | 0      | -    | 0        |
|               | 10 ppm     | 0      | 0           | 0        | 0    | 0      | 0      | 0        | 0      | 0      | 0    | 0    | -      | 0    | 0        |
|               | 30 ppm     | 0      | Õ           | ŏ        | 0    | 0      | 0      | 0        | 0      | 0      | -    |      | 0      | 0    | 0        |
|               | oo ppm     | U      | v           | v        | U    | v      | U      | U        | U      | U      | 0    | 0    | 0      | 0    | 0        |
| I. PERI MOUTH | 0 ppm      | 0      | 0           | 0        | 0    | 0      | 0      | 0        | 0      | 0      | 0    | 0    | 0      | 0    | 0        |
|               | 3 ppm      | 0      | 0           | 0        | 0    | 0      | 0      | 0        | 0      | 0      | 0    | 0    | 0      | õ    | õ        |
|               | 10 ppm     | 0      | 0           | 0        | 0    | 0      | 0      | 0        | 0      | 0      | 0    | Õ    | ů<br>0 | õ    | 0<br>0   |
|               | 30 ppm     | 0      | 0           | 0        | 0    | 0      | 0      | 0        | 0      | 0      | Ő    | õ    | ů.     | õ    | 0        |
| LORAL CAVITY  | 0 ppm      | 0      | 0           | 0        | 0    | 0      | 0      | 0        | 0      | 0      | 0    | 0    | 0      | 0    | 0        |
|               | 3 ppm      | 0      | 0           | 0        | 0    | 0      | 0      | 0        | Õ      | ŏ      | ŏ    | õ    | Ő      | õ    | 0        |
|               | 10 ppm     | 0      | 0           | 0        | 0    | Ő      | õ      | 0        | õ      | õ      | 0    | 0    | 0      | 0    | 0        |
|               | 30 ppm     | 0      | 0           | 0        | 0    | 0      | 0      | 0        | õ      | ŏ      | 0    | 0    | 0      | 0    | 0        |
| I. MANDIBULAR | 0 ppm      | 0      | 0           | 0        | 0    | 0      | 0      | 0        | 0      | 0      | 0    | 0    | 0      | 0    | <u>_</u> |
|               | 3 ppm      | 0      | 0<br>0      | Õ        | 0    | 0      | 0      | 0        | .0     | 0      | 0    | 0    | 0      | 0    | 0        |
|               | 10 ppm     | Ő      | Ő           | õ        | 0    | Ő      | 0      | 0        | 0      | 0      | 0    | -    | 0      | 0    | 0        |
|               | 30 ppm     | 0      | 0           | 0        | 0    | 0      | 0      | 0        | 0      | 0      | 0    | 0    | 0<br>0 | 0    | 0<br>0   |
| I. EAR        | mqq 0      | 0      | 0           | 0        | 0    | 0      | 0      | 0        | 0      | 0      | ^    | ^    | ^      | ^    | <u>^</u> |
|               | a pom      | Ő      | Õ           | ŏ        | 0    | 0      | 0      | 0        | 0      | 0      | 0    | 0    | 0      | 0    | 0        |
|               | 10 ppm     | 0      | 0           | 0        | 0    | 0      | 0      | 0        | -      | -      | 0    | 0    | 0      | 0    | 0        |
|               | 30 ppm     | 0      | 0           | 0        | 0    | 0      | 0      | 0        | 0<br>0 | 0<br>0 | 0    | 0    | 0<br>0 | 0    | 0<br>0   |
| I. PERI EAR   | 0 ppm      | 0      | 0           | 0        | 0    | 0      | 0      | <u>^</u> | •      |        |      |      | -      |      |          |
|               | 3 ppm      | 0      | 0           | 0        | 0    | 0      | 0      | 0<br>0   | 0      | 0      | 0    | 0    | 0      | 0    | 0        |
|               | 10 ppm     | 0      | 0           | 0        | 0    | 0      | 0      | -        | 0      | 0      | 0    | 0    | 0      | 0    | 0        |
|               | 30 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        |

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CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

-1

#### SEX : MALE

PAGE : 19

| Clinical sign  | Group Name      | Admini | istration 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   | 40-7 | 41-7   | 42-7     |
|                |                 | 1      | 1           | 1       | 1    | 1      | 1      | 1      | 1      | 1        | 1        | 1      | 1    | 1      | 1        |
| INTERNAL MASS  | 0               | 0      | 0           | 0       | 0    | •      | 0      | 0      | 0      | <u>^</u> | <u>^</u> | 0      | 0    | 0      | <u>^</u> |
| INTERNAL MASS  | 0 ppm           | 0<br>0 | 0<br>0      | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
|                | 3 ppm           |        | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
|                | 10 ppm          | 0<br>0 | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
|                | 30 ppm          | U      | U           | 0       | U    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
| I. NOSE        | 0 ppm           | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
|                | 3 ppm           | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
|                | 10 ppm          | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
|                | 30 ppm          | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
| I. EYE         | 0 ppm           | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
|                | 3 ppm           | Ő      | õ           | 0       | 0    | Ő      | õ      | 0      | 0      | õ        | õ        | 0      | 0    | 0      | 0        |
|                | 10 ppm          | 0      | 0           | 0       | 0    | 0<br>0 | 0<br>0 | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
|                | 30 ppm          | 0      | Ő           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | õ        | 0      | 0    | 0      | 0        |
|                | •               | •      |             |         |      |        |        |        |        |          |          |        |      |        |          |
| A. PERI MOUTH  | 0 ppm           | 0      | 0           | 0       | 0    | 0      | 0      | 0.     | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
|                | 3 ppm           | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
|                | 10 ppm          | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
|                | 30 ppm          | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
| M. ORAL CAVITY | 0 ppm           | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
|                | 3 ppm           | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
|                | 10 ppm          | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
|                | 30 ppm          | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
| M. MANDIBULAR  | 0 ppm           | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
|                | 3 ppm           | õ      | 0<br>0      | ů       | ů    | õ      | Ő      | 0<br>0 | 0      | 0        | 0        | 0      | 0    | Ő      | 0        |
|                | 10 ppm          | 0      | Ő           | 0<br>0  | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
|                | 30 ppm          | 0      | 0           | 0<br>0  | õ    | 0      | Õ      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
| V. EAR         | 0 ppm           | 0      | 0           | 0       | 0    | 0      | 0      | 0      | ,      | 1        | 4        |        |      | 1      |          |
| (1+ 151 LET    | 0 ppm<br>3 ppm  | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 1<br>0 | 1<br>0   | 1<br>0   | 1<br>0 | 1 0  | 1<br>0 | 1        |
|                | 3 ppm<br>10 ppm | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      |      |        | 0        |
|                |                 | 0      | 0           | 0       | 0    | 0      | 0      |        |        |          |          |        | 0    | 0      | 0        |
|                | 30 ppm          | U      | U           | U       | U    | U      | U      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
| M. PERI EAR    | 0 mqq           | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
|                | 3 ppm           | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
|                | 10 ppm          | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |
|                | 30 ppm          | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0        | 0        | 0      | 0    | 0      | 0        |

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CLINICAL OBSERVATION (SUMMARY)

#### SEX : MALE

PAGE : 20

| 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 |
|               | ·····           | 1      | 1          | 1       | 1      | 1      | 1             | 1    | 1    | 1      | 1    | 1      | 1      | 1      | 1    |
| NTERNAL MASS  | 0 ppm           | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
| NIDRARD MICO  | 3 ppm           | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0<br>0 | 0<br>0 | 0      | 0    |
|               | 10 ppm          | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | Û      | 0    | 0      |        | 0      | 0    |
|               | 30 ppm          | 0      | õ          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0<br>0 | 0<br>0 | 0    |
| . NOSE        | 0 ppm           | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
|               | 3 ppm           | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
|               | 10 ppm          | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | Ō      | 0    | Õ      | ů.     | Õ      | õ    |
|               | 30 ppm          | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
| . EYE         | 0 ppm           | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
|               | 3 ppm           | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
|               | 10 ppm          | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
|               | 30 ppm          | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
| PERI MOUTH    | 0 ppm           | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
|               | 3 ppm           | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
|               | 10 ppm          | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
|               | 30 ppm          | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
| ORAL CAVITY   | 0 ppm           | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
|               | 3 ppm           | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | . 0    | 0    |
|               | 10 ppm          | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
|               | 30 ppm          | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
| . MANDIBULAR  | 0 ppm           | 0      | 0.         | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
|               | 3 ppm           | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
|               | 10 ppm          | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
|               | 30 ppm          | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
| L EAR         | 0 ppm           | 1      | 1          | 1       | 1      | 1      | 1             | 1    | 1    | 1      | 1    | 1      | 1      | 1      | 1    |
|               | 3 ppm           | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
|               | 10 ppm          | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
|               | 30 ppm          | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
| LPERI EAR     | 0 ppm           | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
|               | 3 ppm<br>10 ppm | 0<br>0 | 0<br>0     | 0<br>0  | 0<br>0 | 0<br>0 | 0             | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    |
|               | 30 ppm          | 0      | 0          | 0       | 0      | 0      | 0             | 0    | 0    | 0<br>0 | 0    | 0      | 0      | 0      | 1    |
|               | 30 ppm          | U      | U          | U       | U      | v      | U             | U    | U    | U      | U    | U      | 0      | 0      | 0    |

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CLINICAL OBSERVATION (SUMMARY)

### SEX : MALE

PAGE : 21

| Clinical sign  | Group Name       | Admini | istration N | 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     |
|                |                  | 1      | 1           | 1         | 1      | 1    | 1        | 1    | 1    | 1        | 1    | 1        | 1    | 1    | 1        |
| INTERNAL MASS  | 0                | 0      | 0           | 0         | 0      | 0    | <u>^</u> | 0    | 0    | <u>^</u> |      | 0        | 0    |      | <u>^</u> |
| INTERNAL RAGO  | 0 ppm            |        |             |           | 0      | 0    | 0        | 0    | 0    | 0        | 1    | 0        | 0    | 0    | 0        |
|                | 3 ppm            | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |
|                | 10 ppm           | 0<br>0 | · 0<br>0    | 0         | 0      | 0    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |
|                | 30 ppm           | 0      | U           | U         | U      | U    | 0        | U    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |
| I. NOSE        | 0 ppm            | 0      | . 0         | 0         | 0      | 0    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |
|                | 3 ppm            | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |
|                | 10 ppm           | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |
|                | 30 ppm           | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | Õ        | 0    | Ő        | õ    | 0    | 0        |
| M. EYE         | 0 ppm            | 0      | ^           | ^         | ^      | ^    | ^        | 0    | 0    | •        | •    | <u>^</u> | •    | •    | •        |
| Nie 1 1 1      |                  | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |
|                | 3 ppm            | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |
|                | 10 ppm           | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |
|                | 30 ppm           | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |
| M. PERI MOUTH  | 0 ppm            | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |
|                | 3 ppm            | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | 1        | 1    | 0        | 0    | 0    | 0        |
|                | 10 ppm           | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |
|                | 30 ppm           | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | . 0      |
| M. ORAL CAVITY | 0 ppm            | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |
|                | 3 ppm            | 0      | 0           | 0<br>0    | 0      | 0    | 0<br>0   | 0    | 0    | 0        | 0    | 0        | 0    | 0    |          |
|                | 10 ppm           | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | 0        |      | -        |      |      | 0        |
|                | 30 ppm           | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |
|                | oo ppm           | v      | v           | U         | U      | U    | U        | U    | U    | U        | U    | 0        | 2    | 2    | 2        |
| M. MANDIBULAR  | 0 ppm            | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |
|                | 3 ppm            | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |
|                | 10 ppm           | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |
|                | 30 ppm           | 0      | 0           | 0         | 0      | 0    | 1        | 1    | 1    | 1        | 1    | 1        | 1    | 1    | 1        |
| M. EAR         | 0 ppm            | 1      | t           | 1         | 1      | 1    | 1        | 2    | 2    | 2        | 2    | 2        | 2    | 2    | 2        |
|                | 3 ppm            | 0      | 0           | 1         | 1      | 1    | 1        | 0    | 0    | 0        | 2    | 0        | 2    | 2    | 0        |
|                | 10 ppm           | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |
|                | 30 ppm           | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |
|                |                  |        | _           |           |        |      |          |      |      |          |      |          |      |      | -        |
| M. PERI EAR    | 0 ppm            | 0      | 0           | 0         | 0      | 0    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |
|                | 3 ppm            | 0      | 0           | 0         | 0      | 0    | 0        | 1    | 1    | 1        | 1    | 1        | 1    | 1    | 1        |
|                | 10 ppm<br>20 ppm | 1      | 1<br>0      | 1<br>0    | 1<br>0 | 1    | 1        | 1    | 1    | 1        | 1    | 1        | 1    | 1    | 1        |
|                | 30 ppm           | U      | U           | U         | U      | U    | 0        | 0    | 0    | 0        | 0    | 0        | 0    | 0    | 0        |

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CLINICAL OBSERVATION (SUMMARY)

#### SEX : MALE

PAGE : 22

| Clinical sign | Group Name      | Admini   | stration W | eek-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 |
|               |                 | 1        | 1          | 1       | 1      | 1      | 1      | 1      | 1    | 1    | 1                                      | 1    | 1      | 1    | 1    |
| NTERNAL MASS  | 0               | <u>,</u> | •          |         |        | _      |        |        |      |      |                                        |      |        |      |      |
| NIENNAL MASS  | 0 ppm           | 0        | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0                                      | 1    | 0      | 0    | 0    |
|               | 3 ppm           | 0        | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0                                      | 0    | 0      | 0    | 0    |
|               | 10 ppm          | 0        | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0                                      | 0    | 0      | 0    | 0    |
|               | 30 ppm          | 0        | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0                                      | 0    | 0      | 0    | 0    |
| . NOSE        | 0 ppm           | 0        | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0                                      | 0    | 0      | 0    | 0    |
|               | 3 ppm           | 0        | 0          | 1       | 1      | ĩ      | 1      | 1      | ĩ    | 1    | 1                                      | 1    | 1      | 1    | 1    |
|               | 10 ppm          | 0        | 0          | ō       | õ      | Ô      | 0<br>0 | Ō      | 0    | 0    | 0                                      | 0    | 0      | 0    | 0    |
|               | 30 ppm          | 0        | 0          | 0       | 0      | 0      | 0      | 0      | Ő    | õ    | 0                                      | 0    | 0      | 0    | 0    |
| I. EYE        | 0               | •        | •          | •       |        |        |        |        |      |      |                                        |      |        | -    | -    |
|               | 0 ppm           | 0        | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0                                      | 0    | 0      | 0    | 0    |
|               | 3 ppm           | 0        | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0                                      | 0    | 0      | 0    | 0    |
|               | 10 ppm          | 0        | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0                                      | 0    | 0      | 0    | 0    |
|               | 30 ppm          | 0        | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0                                      | 0    | 0      | 0    | 0    |
| I. PERI MOUTH | mqq 0           | 0        | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0                                      | 0    | 0      | 0    | 0    |
|               | 3 ppm           | 0        | 0          | 0       | 0      | 0      | 0      | Ő      | õ    | õ    | 0                                      | õ    | 0      | 0    | 0    |
|               | 10 ppm          | 0        | 0          | 0       | 0      | 0 .    | õ      | õ      | Ő    | Ő    | 0                                      | 0    | 0      | 0    | 0    |
|               | 30 ppm          | 0        | 0          | 0       | 0      | 1      | 1      | 1      | 1    | 1    | 1                                      | 1    | 1      | 1    | 1    |
| LORAL CAVITY  | 0 ppm           | 0        | 0          | 0       | 0      | 0      | •      | â      |      |      |                                        |      |        |      |      |
|               | 3 ppm           | 0        | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0                                      | 0    | 0      | 0    | 0    |
|               | 3 ppm<br>10 ppm | 0        | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0                                      | 0    | 0      | 0    | 0    |
|               | 30 ppm          | 2        | 1          | 1       | 0<br>1 | 0<br>1 | 0      | 0      | 0    | 0    | 0                                      | 0    | 0      | 0    | 0    |
|               | oo ppu          | 2        | T          | T       | 1      | 1      | 1      | 1      | 1    | 1    | 1                                      | 0    | 0      | 0    | 0    |
| I. MANDIBULAR | 0 ppm           | 0        | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0                                      | 0    | 0      | 0    | 0    |
|               | 3 ppm           | 0        | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0                                      | 0    | 0      | 0    | Ő    |
|               | 10 ppm          | 0        | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0                                      | 0    | 0      | 0    | Ő    |
|               | 30 ppm          | 1        | 1          | 1       | 1      | 1      | 1      | 1      | 1    | 1    | 1                                      | 1    | 1      | 1    | 1    |
| I. EAR        | 0 ppm           | 2        | 2          | 2       | 2      | 2      | 2      | n      | 0    | 0    | 0                                      |      |        | 0    |      |
|               | 3 ppm           | 0        | 0          | 0       | 0      | 2      | 0      | 2<br>0 | 2    | 2    | 2                                      | 2    | 2      | 2    | 2    |
|               | 10 ppm          | 0        | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0                                      | 0    | 0      | 0    | 0    |
|               | 30 ppm          | 0        | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0                                      | 0    | 0<br>0 | 0    | 0    |
|               |                 |          |            |         | -      | -      | Ť      | Ť      | Ý    | v    | v                                      | v    | v      | U    | U    |
| L PERI EAR    | 0 ppm           | 0        | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0                                      | 0    | 0      | 0    | 0    |
|               | 3 ppm           | 1        | 1          | 1       | 1      | 1      | 1      | 1      | 0    | 0    | 0                                      | 0    | 0      | 0    | 0    |
|               | 10 ppm          | 1        | 1          | 1       | 1      | 1      | 1      | 1      | 1    | 1    | 0                                      | 0    | 0      | 0    | 0    |
|               | 30 ppm          | 0        | 0          | 0       | 0      | 1      | 1      | 1      | 1    | 1    | 1                                      | 1    | 1      | 1    | 1    |

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CLINICAL OBSERVATION (SUMMARY)

#### SEX : MALE

PAGE : 23

| 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   |
|               |                 |        | 1          | 1       | 1    | 1    | 1    | 1      | 1    | 1    | 1    | 1    | 1    | 1      | 1      |
| TERNAL MASS   | <u>^</u>        |        |            |         |      |      |      |        |      |      |      |      |      |        |        |
| NIGRINAL MASS | 0 ppm           | 1      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 1    | 2    | 1      | 1      |
|               | 3 ppm           | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|               | 10 ppm          | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 1      |
|               | 30 ppm          | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 1      | 2      |
| NOSE          | 0 ppm           | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|               | 3 ppm           | 1      | 1          | 1       | 1    | 1    | 1    | 1      | 1    | 1    | 1    | 1    | 1    | 1      | 1      |
|               | 10 ppm          | Ō      | ō          | 0       | Ô    | Ô    | 0    | 0      | 0    | 0    | 0    | 0    | 0    | -      | -      |
|               | 30 ppm          | 0      | õ          | 0       | õ    | 1    | 1    | 0      | 1    | 2    | 2    | 1    | 1    | 0<br>1 | 0<br>2 |
| . EYE         | •               | ^      | <u>,</u>   | •       |      |      |      | _      |      |      | _    |      | -    | -      | -      |
| . 111         | 0 ppm           | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|               | 3 ppm           | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|               | 10 ppm          | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|               | 30 ppm          | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 1    | 1    | 1    | 1    | 0      | 0      |
| PERI MOUTH    | 0 ppm           | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|               | 3 ppm           | 0      | 0          | 0       | 0    | 0    | 0    | ů<br>0 | õ    | Ô    | 0    | 0    | 0    | 0      | 0      |
|               | 10 ppm          | 0      | 0          | 0       | 0    | 0    | 0    | Õ      | Ő    | 0    | 1    | 2    | 2    | 2      | 2      |
|               | 30 ppm          | 1      | 1          | 1       | 1    | 1    | 1    | 1      | 1    | Ö    | 0    | õ    | 0    | 1      | 1      |
| ORAL CAVITY   | 0.555           | 0      | ^          | 0       | 0    | •    | •    |        |      |      |      |      |      |        |        |
|               | 0 ppm           | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|               | 3 ppm<br>10 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      |
|               | 30 ppm          | U      | Ų          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
| MANDIBULAR    | 0 ppm           | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|               | 3 ppm           | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    | Õ    | õ      | Õ      |
|               | 10 ppm          | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | Õ    | õ    | 0    | 0      | 0      |
|               | 30 ppm          | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | Ō    | õ    | õ    | 0      | 0      |
| EAR           | mqq 0           | 2      | 1          | 1       | 1    |      |      |        |      |      |      |      |      |        |        |
|               | 3 ppm           | 0      | 0          | 1       | 1    | 1    | 1    | 1      | 1    | 1    | 1    | 1    | 1    | 1      | 1      |
|               | 3 ppm<br>10 ppm | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|               | 30 ppm          | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|               | so ppm          | U      | U          | v       | U    | 0    | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
| PERI EAR      | 0 ppm           | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|               | 3 ppm           | 0      | 0          | 0       | 0    | 0    | 0    | 1      | 1    | 1    | õ    | õ    | 0    | 0<br>0 | 0      |
|               | 10 ppm          | 0      | 0          | 0       | 0    | 0    | 0    | 1      | Ō    | Ō    | Õ    | õ    | 0    | 0      | 0      |
|               | 30 ppm          | 1      | 1          | 1       | 0    | 0    | 0    | 0      | 0    | 1    | 1    | ĩ    | 1    | 1      | 1      |

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CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : MALE

PAGE : 24

| Clinical sign | Group Name | Admin  | istration | Week-day |        |       |       |      | <br> |
|---------------|------------|--------|-----------|----------|--------|-------|-------|------|------|
|               |            | 99-7   | 100-7     | 101-7    | 102-7  | 103-7 | 104-7 |      |      |
|               |            | 1      | 1         | 1        | 1      | 1     | 1     | <br> |      |
| NTERNAL MACC  |            |        |           |          |        |       |       |      |      |
| NTERNAL MASS  | mqq 0      | 1      | 1         | 1        | 0      | 0     | 1     |      |      |
|               | 3 ppm      | 0      | 0         | 0        | 0      | 0     | 0     |      |      |
|               | 10 ppm     | 1      | 1         | 1        | 1      | 1     | 1     |      |      |
|               | 30 ppm     | 1      | 1         | 1        | 1      | 1     | 1     |      |      |
| I. NOSE       | 0 ppm      | 0      | 0         | 0        | 0      | 0     | 0     |      |      |
|               | 3 ppm      | 1      | 1         | 1        | 1      | 1     | 1     |      |      |
|               | 10 ppm     | 1      | 1         | 1        | 1      | 1     | 1     |      |      |
|               | 30 ppm     | 1      | 1         | 1        | 2      | 1     | 3     |      |      |
| M. EYE        | 0 ppm      | 0      | 0         | 0        | 0      | 0     | 0     |      |      |
|               | 3 ppm      | 0      | 0         | 0        | 0      | 0     | 0     |      |      |
|               | 10 ppm     | 0      | 0         | 0        | 0      | 0     | Ō     |      |      |
|               | 30 ppm     | 0      | 0         | 0        | 0      | 1     | 1     |      |      |
| I. PERI MOUTH | 0 ppm      | 0      | 0         | 0        | 0      | 0     | 0     |      |      |
|               | 3 ppm      | Ő      | õ         | 0        | 0<br>0 | õ     | 0     |      |      |
|               | 10 ppm     | 2      | 2         | 2        | 2      | 2     | 2     |      |      |
|               | 30 ppm     | 2      | 2<br>2    | 2<br>2   | 2      | 2     | 2     |      |      |
| A ORAL CAVITY | 0 ppm      | 0      | 0         | 0        | 0      | 0     | 0     |      |      |
|               | 3 ppm      | 0      | 0         | 0        | 0      | 0     | 0     |      |      |
|               | 10 ppm     | 0<br>0 | 0         | 0        | 0      | Ő     | 0     |      |      |
|               | 30 ppm     | 0      | ŏ         | 0        | 0      | 0     | 0     |      |      |
|               | oo bbu     | Ū      | v         | Ŭ        | 0      | v     | U     |      |      |
| A. MANDIBULAR | 0 ppm      | 0      | 0         | 0        | 0      | 0     | 0     |      |      |
|               | 3 ppm      | 0      | 0         | 0        | 0      | 0     | 0     |      |      |
|               | 10 ppm     | 0      | 0         | 0        | 0      | 0     | 0     |      |      |
|               | 30 ppm     | 0      | 0         | 0        | 0      | 0     | 0     |      |      |
| I. EAR        | 0 ppm      | 1      | 1         | 1        | 1      | 1     | 1     |      |      |
|               | 3 ppm      | 0      | 0         | 0        | 0      | 1     | 0     |      |      |
|               | 10 ppm     | 0      | 1         | 1        | 1      | 0     | 0     |      |      |
|               | 30 ppm     | 0      | 0         | 0        | 0      | 0     | 0     |      |      |
| M. PERI EAR   | 0 ppm      | 0      | 0         | 0        | 0      | 0     | 0     |      |      |
|               | 3 ppm      | 0      | 0         | 0        | 0      | 0     | 0     |      |      |
|               | 10 ppm     | 0      | 0         | 0        | 0      | 0     | 0     |      |      |
|               | 30 ppm     | 1      | 1         | 1        | 1      | 1     | 1     |      |      |

#### SEX : MALE

PAGE : 25

|                    |                 |     |     | 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   |
|                    |                 | 1   | 1   | 1        | 1   | 1   | 1   | 1      | 1   | 1        | 1    | 1    | 1    | 1      | 1      |
| NECK               | 0               | 0   | 0   | <u>^</u> | •   | 0   |     |        |     |          | _    |      |      |        |        |
| . NEOR             | 0 ppm           | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 3 ppm<br>10 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      |
|                    | 30 ppm          | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | 0        | 0    | 0    | 0    | 0      | 0      |
| BREAST             | 0 ppm           | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 3 ppm           | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | 0        | 0    | 0    | 0    | Õ      | õ      |
|                    | 10 ppm          | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | 0        | 0    | 0    | Õ    | Õ      | õ      |
|                    | 30 ppm          | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | 0        | 0    | 0    | 0    | 0      | Õ      |
| L ABDOMEN          | 0 ppm           | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | •        | •    | •    |      | •      |        |
|                    | 3 ppm           | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 10 ppm          | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 30 ppm          | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   |          | 0    | 0    | 0    | 0      | 0      |
|                    | ndd og          | U   | v   | 0        | U   | U   | U   | U      | U   | 0        | 0    | 0    | 0    | 0      | 0      |
| ANTERIOR. DORSUM   | 0 ppm           | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 3 ppm           | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 10 ppm          | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 30 ppm          | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | 0        | 0    | 0    | 0    | 0      | 0      |
| L POSTERIOR DORSUM | 0 ppm           | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | ö        | 0    | 0    | 0    | 0      | 0      |
|                    | 3 ppm           | 0   | õ   | Ő        | Ő   | 0   | Ő   | 0      | 0   | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 10 ppm          | Ő   | Õ   | õ        | Ő   | Ő   | 0   | 0      | 0   | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 30 ppm          | 0   | 0   | 0        | Ő   | 0   | Ő   | 0      | 0   | 0        | 0    | 0    | 0    | 0      | 0<br>0 |
|                    |                 |     |     |          |     |     |     |        |     |          | -    | -    |      | ·      | · ·    |
| . HINDLIMB         | 0 ppm           | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 3 ppm           | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 10 ppm          | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 30 ppm          | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | 0        | 0    | 0    | 0    | 0      | 0      |
| . GENITALIA        | 0 ppm           | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 3 ppm           | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | Ő        | õ    | 0    | õ    | 0      | 0      |
|                    | 10 ppm          | 0   | 0   | 0        | 0   | 0   | Õ   | õ      | õ   | õ        | 0    | Ő    | 0    | 0      | 0      |
|                    | 30 ppm          | 0   | 0   | 0        | 0   | 0   | 0   | 0      | õ   | 0        | Ő    | 0    | 0    | 0      | 0      |
| NEMIA              | 0 ppm           | 0   | 0   | 0        | 0   | 0   | 0   | ~      | ~   | <u>^</u> | ~    | ~    | ~    | -      |        |
|                    | 3 ppm           | 0   | 0   | 0        | 0   | 0   | 0   | 0<br>0 | 0   | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 10 ppm          | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 30 ppm          | 0   | 0   | 0        | 0   | 0   | 0   | 0      | 0   | 0<br>0   | 0    | 0    | 0    | 0<br>0 | 0<br>0 |

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CLINICAL OBSERVATION (SUMMARY)

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STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

SEX : MALE

PAGE : 26

| 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 |
|                     |            | 1    | 1          | 1    | 1    | 1    | 1      | 1    | 1    | 1    | 1      | 1      | 1      | 1    | 1    |
|                     |            |      |            |      |      |      |        |      |      |      |        |        |        |      |      |
| I. NECK             | 0 ppm      | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                     | 3 ppm      | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                     | 10 ppm     | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | Ō      | Ō    | Ō    |
|                     | 30 ppm     | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | ů<br>0 | 0.   | Û    |
| I. BREAST           | 0 ppm      | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                     | 3 ppm      | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | Ő      | Õ      | õ    | õ    |
|                     | 10 ppm     | õ    | ů<br>0     | õ    | 0    | õ    | Ő      | 0    | 0    | 0    | 0<br>0 | Ő      | 0      | 0    | 0    |
|                     | 30 ppm     | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
| K. ABDOMEN          | 0 ppm      | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                     | 3 ppm      | 0    | 0          | 0    | 0    | 0    | 0      | 0    | õ    | õ    | ů<br>0 | ů<br>0 | 0      | Ő    | õ    |
|                     | 10 ppm     | Ő    | õ          | Ő    | õ    | 0    | 0<br>0 | 0    | Õ    | õ    | ŏ      | 0      | 0      | . 0  | 0    |
|                     | 30 ppm     | 0    | õ          | Ő    | 0    | õ    | Ő      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                     | 00 101     | Ŭ    | Ū          | v    | Ū    | v    | v      | 0    | Ū    | Ū    | U      | 0      | 0      | U    | U    |
| ANTERIOR. DORSUM    | 0 ppm      | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                     | 3 ppm      | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                     | 10 ppm     | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                     | 30 ppm     | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
| A. POSTERIOR DORSUM | 0 ppm      | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                     | 3 ppm      | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                     | 10 ppm     | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                     | 30 ppm     | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
| M. HINDLIMB         | 0 ppm      | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                     | 3 ppm      | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                     | 10 ppm     | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                     | 30 ppm     | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
| M. GENITALIA        | 0 ppm      | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                     | 3 ppm      | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                     | 10 ppm     | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                     | 30 ppm     | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | Õ      | õ      | Ö      | õ    | 0    |
| ANEMIA              | 0 ppm      | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                     | 3 ppm      | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                     | 10 ppm     | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0      | õ    | õ    |
|                     | 30 ppm     | 0    | 0          | 0    | 0    | 0    | 0      | 0    | 0    | 0    | Ő      | õ      | Õ      | ő    | õ    |

CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

#### SEX : MALE

PAGE : 27

| Clinical sign       | Group Name |      | stration W |      |      |      |      |      |          |          |      |      |          |          |      |
|---------------------|------------|------|------------|------|------|------|------|------|----------|----------|------|------|----------|----------|------|
|                     |            | 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 |
|                     |            | 1    | 1          | 1    | 1    | 1    | 1    | 1    | 1        | 1        | 1    | 1    | 1        | 1        | 1    |
| . NECK              | 0          | 0    | 0          | 0    | 0    | 0    | 0    | 0    | <u>^</u> | <u>^</u> | 0    | 0    | <u>^</u> | <u>^</u> | 0    |
| L NECK              | 0 ppm      | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
|                     | 3 ppm      | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
|                     | 10 ppm     | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | . 0      | 0        | 0    |
|                     | 30 ppm     | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
| . BREAST            | 0 ppm      | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 1    |
|                     | 3 ppm      | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
|                     | 10 ppm     | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
|                     | 30 ppm     | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
| I. ABDOMEN          | 0 ppm      | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
|                     | 3 ppm      | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
|                     | 10 ppm     | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
|                     | 30 ppm     | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
| ANTERIOR. DORSUM    | 0 ppm      | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
|                     | 3 ppm      | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
|                     | 10 ppm     | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
|                     | 30 ppm     | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
| I. POSTERIOR DORSUM | 0 ppm      | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
|                     | 3 ppm      | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
|                     | 10 ppm     | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
|                     | 30 ppm     | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
| I. HINDLIMB         | 0 ppm      | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
|                     | 3 ppm      | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
|                     | 10 ppm     | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
|                     | 30 ppm     | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
| 1. GENITALIA        | 0 ppm      | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
|                     | 3 ppm      | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
|                     | 10 ppm     | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
|                     | 30 ppm     | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
| ANEMIA              | 0 ppm      | 0    | 0          | 0    | 0    | 0    | 0    | 0    | 0        | 0        | 0    | 0    | 0        | 0        | 0    |
|                     | 3 ppm      | 0    | 0          | 0    | 0    | 0    | 0    | 0    | Ő        | 0        | 0    | õ    | 0        | õ        | ů    |
|                     | 10 ppm     | 0    | 0          | 0    | 0    | Ō    | Ō    | Ő    | Ő        | õ        | õ    | õ    | Õ        | Ő        | Ő    |
|                     | 30 ppm     | 0    | 0          | 0    | õ    | 0    | Ő    | õ    | 0        | õ        | 0    | 0    | õ        | õ        | 0    |

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CLINICAL OBSERVATION (SUMMARY)

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CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

SEX : MALE

PAGE : 28

|                    | Group Name | numii) | istration 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 |
|                    | ·          | 1      | 1           | 1       | 1      | 1    | 1      | 1      | 1      | 1      | 1    | 1      | 1      | 1    | 1    |
| I. NECK            | 2          | 0      | Â           | 0       |        |      |        | _      |        |        |      |        |        |      |      |
| 1. NECK            | 0 ppm      | 0      | 0           | 0       | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0    |
|                    | 3 ppm      | 0      | 0           | 0       | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0    |
|                    | 10 ppm     | 0      | 0           | 0       | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0    |
|                    | 30 ppm     | 0      | 0           | 0       | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0    |
| 4. BREAST          | 0 ppm      | 1      | 1           | 1       | 1      | 1    | 1      | 1      | 1      | 1      | 1    | 1      | 1      | 1    | 1    |
|                    | 3 ppm      | 0      | 0           | 0       | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0    |
|                    | 10 ppm     | 0      | 0           | 0       | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0    |
|                    | 30 ppm     | 0      | 0           | 0       | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0    |
| I. ABDOMEN         | 0 ppm      | 0      | 0           | 0       | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0    |
|                    | 3 ppm      | 0      | 0           | 0       | 0      | 0    | Ő      | Õ      | õ      | õ      | Ő    | ŏ      | 0<br>0 | 0    | 0    |
|                    | 10 ppm     | õ      | Õ           | õ       | õ      | 1    | 2      | 2      | 2      | 2      | 2    | 2      | 2      | 2    | 2    |
|                    | 30 ppm     | 0      | 0           | õ       | õ      | Ô    | 0      | 0      | õ      | ő      | 0    | 0      | 0      | 0    | 0    |
| ANTERIOR. DORSUM   | 0 ppm      | 0      | 0           | 0       | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0    |
|                    | 3 ppm      | 0      | 0           | 0       | 0      | ŏ    | õ      | ů<br>0 | õ      | 0<br>0 | 0    | 0      | 0      | 0    | 0    |
|                    | 10 ppm     | ů<br>0 | õ           | 0       | Ő      | 0    | 0<br>0 | 0      | 0      | ŏ      | 0    | -      |        |      |      |
|                    | 30 ppm     | 0      | 0           | 0       | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0<br>0 | 0    | 0    |
|                    | 30 ppm     | 0      | 0           | v       | 0      | U    | Ū      | U      | U      | U      | U    | 0      | U      | 0    | 0    |
| L POSTERIOR DORSUM | 0 ppm      | 0      | 0           | 0       | 1      | 1    | 1      | 1      | 1      | 1      | 1    | 1      | 1      | 1    | 1    |
|                    | 3 ppm      | 0      | 0           | 0       | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0    |
|                    | 10 ppm     | 0      | 0           | 0       | 0      | 0    | 0      | 0      | 0      | 0      | 0    | Ó      | 0      | Ō    | 0    |
|                    | 30 ppm     | 0      | 0           | 0       | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0    |
| I. HINDLIMB        | 0 ppm      | 0      | 0           | 0       | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0    |
|                    | 3 ppm      | 0      | 0           | 0       | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0    |
|                    | 10 ppm     | 0      | 0           | 0       | 0      | 0    | 0      | 0      | Õ      | Õ      | Ő    | õ      | ů<br>0 | Õ    | 0    |
|                    | 30 ppm     | 0      | 0           | 0       | õ      | 0    | ō      | 0<br>0 | 0      | õ      | o    | 0<br>0 | 0      | 0    | 0    |
| I. GENITALIA       | 0 ppm      | 0      | 0           | 0       | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0    |
|                    | 3 ppm      | 0      | 0           | õ       | 0<br>0 | Õ    | õ      | 0      | 0<br>0 | 0      | ŏ    | 0      | 0      | 0    | 0    |
|                    | 10 ppm     | Ő      | Ő           | õ       | õ      | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0    |
|                    | 30 ppm     | 0      | Ő           | 0       | õ      | 0    | 0      | Ő      | Ő      | 0      | 0    | 0      | 0      | 0    | 0    |
| INEMIA             | 0 ppm      | 0      | 0           | 0       | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0    |
|                    | 3 ppm      | õ      | 0           | õ       | ů<br>0 | Õ    | õ      | Ő      | 0      | õ      | 0    | Ő      | 0      | ŏ    | 0    |
|                    | 10 ppm     | õ      | 0           | Ő       | 0      | 0    | 0<br>0 | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0    |
|                    | 30 ppm     | õ      | 0           | õ       | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0    |

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#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

SEX : MALE

PAGE : 29

| Clinical sign                         | Group Name | Administration Week-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   |
|                                       |            | 1                       | 1      | 1      | 1      | 1    | 1      | 1      | 1      | 1      | 1    | 1    | 1    | 1    | 1      |
|                                       |            |                         |        |        |        |      |        |        |        |        |      |      |      |      |        |
| 4. NECK                               | 0 ppm      | 0                       | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      |
|                                       | 3 ppm      | 0                       | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 1    | 1    | 1      |
|                                       | 10 ppm     | 0                       | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      |
|                                       | 30 ppm     | 0                       | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      |
| I. BREAST                             | 0 ppm      | 1                       | 1      | 1      | 1      | 1    | 1      | 1      | 1      | 1      | 1    | 1    | 1    | 1    | 1      |
|                                       | 3 ppm      | 0                       | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      |
|                                       | 10 ppm     | 0                       | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      |
|                                       | 30 ppm     | 0                       | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 1      | 1    | 2    | 2    | 2    | 2      |
| N. ABDOMEN                            | 0 ppm      | 0                       | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 1    | 1    | 1    | 1      |
| · · · · · · · · · · · · · · · · · · · | 3 ppm      | 0                       | Ő      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      |
|                                       | 10 ppm     | 2                       | 2      | 2      | 2      | 2    | 2      | 2      | 2      | 2      | 2    | 2    | 2    | 2    | 2      |
|                                       | 30 ppm     | 0                       | 1      | 1      | 1      | 1    | 1      | 1      | 1      | 1      | 1    | 1    | 1    | 1    | 1      |
| M. ANTERIOR. DORSUM                   | 0 ppm      | 0                       | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0    | ^      |
| a. Tevillarion. Donoom                | 3 ppm      | 0                       | 0      | 0      | 0      | 0    | 0      | · 0    | 0      | 0      | 0    | 0    | 0    | 0    | 0<br>0 |
|                                       | 10 ppm     | 0                       | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      |
|                                       | 30 ppm     | 0                       | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      |
|                                       | oo ppm     | 0                       | v      | Ū      | Ū      | 0    | v      | v      | v      | Ŭ      | v    | U    | v    | U    | Ū      |
| M. POSTERIOR DORSUM                   | 0 ppm      | 1                       | 1      | 1      | 1      | 2    | 1      | 1      | 1      | 1      | 1    | 1    | 1    | 1    | 1      |
|                                       | 3 ppm      | 0                       | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 1    | 1    | 1    | 1      |
|                                       | 10 ppm     | 0                       | 0      | 0      | 1      | 1    | 1      | 1      | 1      | 1      | 1    | 1    | 1    | 1    | 1      |
|                                       | 30 ppm     | 0                       | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 1    | 1    | 1    | 1      |
| M. HINDLIMB                           | 0 ppm      | 0                       | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      |
|                                       | 3 ppm      | 0                       | 0      | Ō      | Ő      | Õ    | õ      | Ő      | õ      | õ      | õ    | õ    | Ő    | õ    | 0<br>0 |
|                                       | 10 ppm     | 0                       | 0      | 0      | 0      | 0    | 0      | 0      | Õ      | Õ      | õ    | õ    | Õ    | õ    | ů<br>0 |
|                                       | 30 ppm     | 0                       | 0      | 0      | 0      | 0    | 0      | 0      | 0      | Ő      | Ő    | õ    | 0    | ů    | 0<br>0 |
| A GENITALIA                           | 0 ppm      | 0                       | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      |
|                                       | 3 ppm      | õ                       | 0<br>0 | ů      | 0      | õ    | 0<br>0 | 0      | 0      | õ      | 0    | 0    | 1    | 1    | 1      |
|                                       | 10 ppm     | õ                       | Ő      | õ      | 0<br>0 | ŏ    | õ      | õ      | 0      | ŏ      | 0    | 0    | 0    | 0    | 0      |
|                                       | 30 ppm     | 0                       | Ő      | 0<br>0 | 0      | 0    | õ      | 0<br>0 | ů<br>0 | 0<br>0 | 0    | 0    | 0    | 0    | 0      |
| ANEMIA                                | 0 ppm      | 0                       | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 1    | 0    | 0    | 0    | 0      |
| # 35 *4.4413.42.8 B                   | 3 ppm      | 0                       | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 1    | 0    | 0.   | 0    | 0      |
|                                       | 10 ppm     | 0                       | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      |
|                                       | 30 ppm     | ů<br>0                  | õ      | õ      | Õ      | Ő    | 0      | 0      | ŏ      | õ      | 0    | õ    | 0    | Ő    | 0      |

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : MALE

PAGE : 30

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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   | 78-7   | 79-7 | 80-7 | 81-7 | 82-7 | 83-7   | 84-7   |
|                    |                  | 1      | 1          | 1        | 1    | 1    | 1      | 1      | 1      | 1    | 1    | 1    | 1    | 1      | 1      |
|                    |                  |        |            |          |      |      |        |        |        |      |      |      |      |        |        |
| 4. NECK            | 0 ppm            | 0      | 0          | 0        | 0    | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 3 ppm            | 1      | 1          | 1        | 1    | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 10 ppm           | 0      | 0          | 0        | 0    | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 30 ppm           | 0      | 0          | 0        | 0    | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      | 0      |
| . BREAST           | 0 ppm            | 1      | 1          | 1        | 1    | 1    | 1      | 1      | 1      | 0    | 0    | 0    | 0    | 2      | 2      |
|                    | 3 ppm            | 0      | 0          | 0        | 0    | 1    | 1      | 1      | 1      | 1    | 1    | 1    | 1    | 1      | 1      |
|                    | 10 ppm           | 0      | 1          | 1        | 1    | 1    | 1      | 1      | 1      | 1    | 0    | 0    | 0    | 0      | 0      |
|                    | 30 ppm           | 2      | 2          | 3        | 3    | 3    | 3      | 3      | 3      | 3    | 3    | 3    | 3    | 3      | 3      |
| L ABDOMEN          | 0 ppm            | 1      | 1          | 2        | 2    | 2    | 1      | 0      | 0      | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 3 ppm            | 0      | 0          | 0        | 0    | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 10 ppm           | 2      | 2          | 2        | 2    | 2    | 2      | 2      | 2      | 2    | 1    | 1    | 1    | 1      | 1      |
|                    | 30 ppm           | 1      | I          | 1        | 1    | 0    | · 0    | 0      | ō      | 0    | õ    | ō    | 0    | ō      | 0      |
| ANTERIOR. DORSUM   | 0 ppm            | 0      | 0          | 0        | 0    | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 3 ppm            | Õ      | õ          | ů        | 0    | õ    | Ő      | Ő      | õ      | 0    | 0    | õ    | 0    | õ      | Ő      |
|                    | 10 ppm           | Õ      | 0<br>0     | õ        | Õ    | õ    | Ő      | ů<br>1 | ĩ      | 1    | 0    | 1    | 1    | 2      | 2      |
|                    | 30 ppm           | 0      | 0          | ů<br>0   | õ    | Ő    | õ      | 0      | 0      | Ô    | õ    | Ô    | 1    | 1      | 1      |
| . POSTERIOR DORSUM | 0 ppm            | 1      | 1          | 1        | 1    | 1    | 1      | 1      | 1      | 1    | 1    | 1    | 1    | 1      | 1      |
|                    | 3 ppm            | 1      | 1          | 1        | 1    | 1    | 1      | 1      | 2      | 2    | 2    | 2    | 2    | 2      | 2      |
|                    | 10 ppm           | 1      | 1          | 1        | 2    | 2    | 2      | 2      | 2      | 2    | 2    | 2    | 2    | 2      | 2      |
|                    | 30 ppm           | 0      | 1          | 1        | 1    | 1    | 1      | 1      | 1      | 1    | 1    | 1    | 1    | 1      | 1      |
| I. HINDLIMB        | mqq 0            | 0      | 0          | 0        | 0    | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 3 ppm            | ŏ      | Õ          | 0<br>0   | õ    | 0    | 0<br>0 | ů<br>0 | ů<br>0 | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 10 ppm           | õ      | õ          | 0        | õ    | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 30 ppm           | 0      | 0          | 0        | 0    | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 1    | 1      | 1      |
| A. GENITALIA       | 0 ppm            | 0      | 0          | 0        | 0    | 0    | 0      | 0      | 0      | 0    | . 0  | 0    | 0    | 0      | 0      |
|                    | 3 ppm            | 1      | 1          | 1        | 1    | 1    | 1      | 1      | 1      | 1    | 1    | 1    | 0    | 0      | 1      |
|                    | 10 ppm           | 0      | 0          | 0        | 0    | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 30 ppm           | Ő      | 0          | 0        | 0    | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      | 0      |
| NEMIA              | 0 ppm            | 0      | 0          | 0        | 0    | 0    | 0      | 0      | 0      | 0    | 0    | 1    | 0    | 0      | ^      |
| an nadmand d       | 3 ppm            | 0      | 0          | 0        | 0    | 0    | 0      | 0      | 0      | 0    | 0    | 1    | 0    | 0<br>0 | 0<br>0 |
|                    | 10 ppm           | 0      | 0          | 0        | 0    | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      |        |
|                    | 10 ррм<br>30 ррм | 0      | 0          | 0        | 0    | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    | 0      | 1<br>0 |
|                    | oo hhii          | U      | v          | v        | 0    | U    | U      | U      | U      | v    | U    | U    | U    | U      | 0      |

### SEX : MALE

PAGE : 31

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| 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 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
|                     |            | 1      | 1           | 1        | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     |            |        |             |          |      |      |      |      |      |      |      |      |      |      |      |
| I. NECK             | 0 ppm      | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    |
|                     | 3 ppm      | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| I. BREAST           | 0 ppm      | 2      | 2           | 2        | 2    | 3    | 3    | 3    | 3    | 3    | 3    | 4    | 4    | 5    | 5    |
|                     | 3 ppm      | 1      | 1           | 1        | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 10 ppm     | 0      | 0           | 0        | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 30 ppm     | 3      | 3           | 3        | 3    | 3    | 3    | 3    | 3    | 3    | 4    | 4    | 4    | 3    | 2    |
| A. ABDOMEN          | 0 ppm      | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    |
|                     | 3 ppm      | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    |
|                     | 10 ppm     | 1      | 1           | 1        | 1    | 2    | 2    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 30 ppm     | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 2    |
| 1. ANTERIOR. DORSUM | 0 ppm      | 0      | 1           | 1        | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 3 ppm      | 0      | 0           | 0        | 1    | 2    | 2    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 10 ppm     | 2      | 2           | 2        | 3    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    |
|                     | 30 ppm     | 1      | 1           | 1        | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
| A POSTERIOR DORSUM  | 0 ppm      | 1      | 1           | 1        | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 3 ppm      | 2      | 2           | 2        | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 3    | 3    |
|                     | 10 ppm     | 2      | 2           | 1        | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 30 ppm     | 1      | 1           | 1        | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
| M. HINDLIMB         | 0 ppm      | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 3 ppm      | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | . 0  | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 1      | 1           | 1        | 1    | 2    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| M. GENITALIA        | 0 ppm      | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 3 ppm      | 1      | 1           | 1        | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 10 ppm     | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| NEMIA               | 0 ppm      | 1      | 0           | 1        | 1    | 1    | 0    | 0    | 0    | 1    | 1    | 0    | 3    | 2    | 2    |
|                     | 3 ppm      | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 1      | 1           | 0        | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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CLINICAL OBSERVATION (SUMMARY)

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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### SEX : MALE

PAGE : 32

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|---------------------|---------------------------------------|------|-------------|-------|-------|-------|-------|--------|
| linical sign        | Group Name                            |      | istration N |       |       |       |       | ۰.<br> |
|                     |                                       | 99-7 | 100-7       | 101-7 | 102-7 | 103-7 | 104-7 |        |
|                     |                                       | 1    | 1           | 1     | 1     | 1     | 1     |        |
|                     |                                       |      |             |       |       |       |       |        |
| I. NECK             | 0 ppm                                 | 1    | 1           | 1     | 1     | 1     | 1     |        |
|                     | 3 ppm                                 | 0    | 0           | 0     | 0     | 0     | 0     |        |
|                     | 10 ppm                                | 0    | 0           | 1     | 0     | 0     | 0     |        |
|                     | 30 ppm                                | 0    | 0           | 0     | 0     | 0     | Ō     |        |
| I. BREAST           | 0 ppm                                 | 6    | 6           | 5     | 5     | 5     | 5     |        |
|                     | 3 ppm                                 | 1    | 1           | 1     | 1     | 1     | 1     |        |
|                     | 10 ppm                                | 0    | Ō           | ō     | Ō     | 1     | 1     |        |
|                     | 30 ppm                                | 1    | 1           | 1     | 1     | 0     | 1     |        |
| I. ABDOMEN          | 0 ppm                                 | 1    | 2           | 2     | 3     | 3     | 3     |        |
|                     | 3 ppm                                 | 1    | 1           | 1     | 2     | 2     | 2     |        |
|                     | 10 ppm                                | 1    | 1           | 1     | 2     | 2     | 2     |        |
|                     | 30 ppm                                | 2    | 2           | 2     | 3     | 3     | 3     |        |
|                     | oo ppm                                | 2    | 4           | 2     | 3     | 3     | 3     |        |
| A. ANTERIOR. DORSUM | 0 ppm                                 | 0    | 0           | 0     | 0     | 0     | 0     |        |
|                     | 3 ppm                                 | 1    | 1           | 1     | 1     | 1     | 1     |        |
|                     | 10 ppm                                | 4    | 4           | 4     | 3     | 3     | 3     |        |
|                     | 30 ppm                                | 1    | 3           | 3     | 5     | 5     | 5     |        |
| A POSTERIOR DORSUM  | 0 ppm                                 | 1    | 1           | 1     | 1     | 1     | 1     |        |
|                     | 3 ppm                                 | 3    | 3           | 3     | 3     | 3     | 3     |        |
|                     | 10 ppm                                | 1    | I           | 1     | 1     | 1     | 1     |        |
|                     | 30 ppm                                | 2    | 2           | 2     | 2     | 2     | 2     |        |
| A. HINDLIMB         | 0 ppm                                 | 0    | 0           | 0     | 0     | 0     | 0     |        |
|                     | 3 ppm                                 | Ő    | õ           | 0     | 0     | 0     | 0     |        |
|                     | 10 ppm                                | õ    | ů<br>0      | 0     | 0     | 0     | 0     |        |
|                     | 30 ppm                                | 1    | 1           | 1     | 1     | 1     | 1     |        |
| I. GENITALIA        | 0 ppm                                 | 0    | 0           | 0     | 0     | 0     | ٥     |        |
|                     | 3 ppm                                 | 1    | 1           |       |       | 0     | 0     |        |
|                     | 3 ppm<br>10 ppm                       | 0    |             | 1     | 1     | 1     | 1     |        |
|                     |                                       |      | 0           | 0     | 0     | 0     | 0     |        |
|                     | 30 ppm                                | 0    | 0           | 0     | 0     | 0     | 0     |        |
| NEMIA               | 0 ppm                                 | 2    | 1           | 0     | 0     | 0     | 0     |        |
|                     | 3 ppm                                 | 0    | 0           | 0     | 0     | 0     | 1     |        |
|                     | 10 ppm                                | 0    | 0           | 0     | 0     | 0     | 0     |        |
|                     | 30 ppm                                | 0    | 0           | 0     | 0     | 0     | 0     |        |

### SEX : MALE

PAGE : 33

| linical sign           | Group Name | Admini | stration W |     |     |        |        |        |     |        |        |        |     |        |        |
|------------------------|------------|--------|------------|-----|-----|--------|--------|--------|-----|--------|--------|--------|-----|--------|--------|
|                        |            | 1-7    | 2-7        | 3-7 | 4-7 | 5-7    | 6-7    | 7-7    | 8-7 | 9-7    | 10-7   | 11-7   | 127 | 13-7   | 14-7   |
|                        |            | 1      | 1          | 1   | 1   | 1      | 1      | 1      | 1   | 1      | 1      | 1      | 1   | 1      | 1      |
| RUSTA                  | •          |        |            |     | _   |        |        |        |     |        |        |        |     |        |        |
| RUSIA                  | 0 ppm      | 0      | 0          | 0   | 0   | 0      | 0      | 0      | 0   | 0      | 0      | 0      | 0   | 0      | 0      |
|                        | 3 ppm      | 0      | 0          | 0   | 0   | 0      | 0      | 0      | 0   | 0      | 0      | 0      | 0   | 0      | 0      |
|                        | 10 ppm     | 0      | 0          | 0   | 0   | 0      | 0      | 0      | 0   | 0      | 0      | 0      | 0   | 0      | 0      |
|                        | 30 ppm     | 0      | 0          | 0   | 0   | 0      | 0      | 0      | 0   | 0      | 0      | 0      | 0   | 0      | 0      |
| ORTICOLLIS             | 0 ppm      | 0      | 0          | 0   | 0   | 0      | 0      | 0      | 0   | 0      | 0      | 0      | 0   | 0      | 0      |
|                        | 3 ppm      | 0      | 0          | 0   | 0   | 0      | 0      | 0      | 0   | 0      | 0      | 0      | 0   | 0      | 0      |
|                        | 10 ppm     | 0      | 0          | 0   | 0   | 0      | 0      | 0      | 0   | 0      | 0      | 0      | 0   | Ő      | 0      |
|                        | 30 ppm     | 0      | 0          | 0   | 0   | 0      | 0      | 0      | 0   | 0      | 0      | 0      | 0   | 0      | 0      |
| RREGULAR BREATHING     | 0 ppm      | 0      | 0          | 0   | 0   | 0      | 0      | 0      | 0   | 0      | 0      | 0      | 0   | 0      | 0      |
|                        | 3 ppm      | 0      | 0          | 0   | 0   | 0      | 0      | 0      | Ő   | õ      | õ      | Õ      | 0   | 0      | 0      |
|                        | 10 ppm     | 0      | 0          | 0   | 0   | 0      | 0      | Ō      | 0   | õ      | õ      | Õ      | Ő   | 0      | 0      |
|                        | 30 ppm     | 0      | 0          | 0   | 0   | 0      | 0      | 0      | 0   | 0      | 0      | ů<br>0 | Ő   | Ő      | 0      |
| IRADYPNEA              | 0 ppm      | 0      | 0          | 0   | 0   | 0      | 0      | 0      | 0   | 0      | 0      | 0      | 0   | 0      | 0      |
|                        | 3 ppm      | 0      | 0          | 0   | 0   | 0      | 0      | 0      | õ   | õ      | · õ    | 0      | 0   | 0<br>0 | 0      |
|                        | 10 ppm     | 0      | 0          | 0   | 0   | 0      | 0      | 0      | Õ   | õ      | Ő      | õ      | 0   | 0      | 0      |
|                        | 30 ppm     | 0      | 0          | 0   | 0   | 0      | 0      | 0      | Õ   | õ      | Ő      | ő      | 0   | 0      | 0      |
| HALLOW BREATHING       | 0 ppm      | 0      | 0          | 0   | 0   | 0      | 0      | 0      | 0   | 0      | 0      | 0      | 0   | 0      | 0      |
|                        | 3 ppm      | 0      | 0          | 0   | 0   | 0      | 0      | Õ      | õ   | ů<br>0 | 0<br>0 | õ      | 0   | 0      | 0      |
|                        | 10 ppm     | 0      | 0          | 0   | õ   | õ      | õ      | 0      | 0   | 0      | 0      | 0      | 0   | 0      | 0      |
|                        | 30 ppm     | 0      | 0          | 0   | 0   | 0      | 0      | ů<br>0 | õ   | Ő      | 0      | 0      | 0   | 0      | 0      |
| BNORMAL RESPIRA. SOUND | 0 ppm      | 0      | 0          | 0   | 0   | 0      | 0      | 0      | 0   | 0      | 0      | 0      | 0   | 0      | 0      |
|                        | 3 ppm      | 0      | 0          | 0   | õ   | Ő      | 0<br>0 | 0      | 0   | 0      | 0      | 0      | 0   | 0      | 0      |
|                        | 10 ppm     | 0      | 0          | 0   | 0   | õ      | 0      | 0      | 0   | 0      | 0      | 0      | 0   | 0      | 0      |
|                        | 30 ppm     | 0      | 0          | 0   | Ō   | Õ      | õ      | 0      | õ   | 0      | 0      | 0      | 0   | 0      | 0      |
| SUBNORMAL TEMP         | 0 ppm      | 0      | 0          | 0   | 0   | 0      | 0      | 0      | 0   | 0      | 0      | 0      | 0   | ^      | 0      |
|                        | 3 ppm      | 0      | Õ          | õ   | õ   | 0      | 0      | 0      | 0   | 0      | 0      | 0      | 0   | 0      | 0      |
|                        | 10 ppm     | Ō      | Õ          | Õ   | õ   | Ő      | 0<br>0 | 0      | Ő   | 0      | 0      | 0      | 0   | 0      | Ŷ      |
|                        | 30 ppm     | 0      | Õ          | õ   | õ   | 0<br>0 | 0      | 0      | 0   | 0      | 0      | 0      | 0   | 0      | 0<br>0 |

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CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

(HAN190)

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### SEX : MALE

PAGE: 34

| Clinical sign          | Group Name | Admini | stration 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 |
|                        |            | 1      | 1          | 1       | 1    | 1    | 1    | 1      | 1    | 1    | 1      | 1      | 1      | 1      | 1    |
|                        |            |        |            |         |      |      |      |        |      |      |        |        |        |        |      |
| CRUSTA                 | 0 ppm      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 3 ppm      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 10 ppm     | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 30 ppm     | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
| ORTICOLLIS             | mqq 0      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 3 ppm      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 10 ppm     | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | õ      | Ő    |
|                        | 30 ppm     | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | õ      | ō      | õ      | 0    |
| RREGULAR BREATHING     | 0 ppm      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 3 ppm      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0<br>0 | 0      | õ      | 0    |
|                        | 10 ppm     | 0      | 0          | 0       | 0    | 0    | 0    | 0      | Ō    | Ō    | Õ      | õ      | 0      | õ      | Ö    |
|                        | 30 ppm     | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | õ      | Ő    |
| BRADYPNEA              | 0 ppm      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 3 ppm      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | õ      | Ő    |
|                        | 10 ppm     | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | Ő      | õ      | Ő    |
|                        | 30 ppm     | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | õ      | õ      | õ      | 0    |
| SHALLOW BREATHING      | 0 ppm      | 0      | 0          | 0       | 0    | 0    | 0    | •      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 3 ppm      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | õ      | õ      | Ő      | õ      | 0    |
|                        | 10 ppm     | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | Õ    | õ      | õ      | 0      | ő      | 0    |
|                        | 30 ppm     | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | ů<br>0 | Ő      | 0      | 0      | 0    |
| BNORMAL RESPIRA. SOUND | mqq 0      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 3 ppm      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | Ō    | Õ    | õ      | 0      | 0<br>0 | 0      | 0    |
|                        | 10 ppm     | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | Ő    | õ      | õ      | 0      | 0      | 0    |
|                        | 30 ppm     | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | ő      | 0      | 0<br>0 | 0    |
| UBNORMAL TEMP          | 0 ppm      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 3 ppm      | 0      | 0          | 0       | 0    | 0    | 0    | Ő      | õ    | Õ    | Ő      | 0      | 0      | 0      | 0    |
|                        | 10 ppm     | 0      | 0          | 0       | 0    | 0    | 0    | Ő      | Ő    | õ    | õ      | 0      | 0      | 0      | 0    |
|                        | 30 ppm     | 0      | 0          | 0       | 0    | 0    | 0    | 0<br>0 | 0    | 0    | 0      | 0      | 0      | 0      | 0    |

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CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

(HAN190)

BAIS 3

### SEX : MALE

PAGE : 35

| Clinical sign          | Group Name | Admin | istration 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 | 40-7 | 41-7   | 42-7   |
|                        |            | 1     | 1           | 1        | 1      | 1    | 1      | 1      | 1      | 1      | 1    | 1    | 1    | 1      | 1      |
|                        |            |       |             |          |        |      |        |        |        |        |      |      |      |        |        |
| CRUSTA                 | 0 ppm      | 0     | 0           | 0        | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      |
|                        | 3 ppm      | 0     | 0           | 0        | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      |
|                        | 10 ppm     | 0     | 0           | 0        | 0      | 0    | 0      | 0      | 0      | 0      | 0    | Ó    | 0    | 0      | Õ      |
|                        | 30 ppm     | 0     | 0           | 0        | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | õ      | 0      |
| TORTICOLLIS            | 0 ppm      | 0     | 0           | 0        | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      |
|                        | 3 ppm      | 0     | 0           | 0        | 0      | 0    | 0      | 0      | 0      | 0      | 0    | Ó    | 0    | 0      | Õ      |
|                        | 10 ppm     | 0     | 0           | 0        | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | õ    | õ      | 0<br>0 |
|                        | 30 ppm     | 0     | 0           | 0        | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      |
| IRREGULAR BREATHING    | 0 ppm      | 0     | 0           | 0        | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      |
|                        | 3 ppm      | 0     | 0           | 0        | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | Õ    | 0<br>0 | Ő      |
|                        | 10 ppm     | 0     | 0           | 0        | 0      | 0    | 0      | 0      | 0      | 0      | 0    | Õ    | Õ    | õ      | Ő      |
|                        | 30 ppm     | 0     | 0           | 0        | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | Ő    | 0<br>0 | 0      |
| BRADYPNEA              | 0 ppm      | 0     | 0           | 0        | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | Û      |
|                        | 3 ppm      | 0     | 0           | 0        | 0      | 0    | 0      | 0      | 0      | õ      | õ    | õ    | 0    | Ő      | 0      |
|                        | 10 ppm     | 0     | 0           | 0        | 0      | 0    | 0      | 0      | õ      | õ      | 0    | 0    | 0    | 0      | 0      |
|                        | 30 ppm     | 0     | 0           | 0        | 0      | 0    | 0      | 0      | 0      | õ      | 0    | 0    | 0    | 0      | 0      |
| SHALLOW BREATHING      | 0 ppm      | 0     | 0           | 0        | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      |
|                        | 3 ppm      | 0     | 0           | 0        | 0      | 0    | 0      | 0<br>0 | Ő      | õ      | 0    | 0    | 0    | 0      | 0      |
|                        | 10 ppm     | 0     | 0           | 0        | 0      | Õ    | Õ      | Ő      | õ      | 0      | 0    | 0    | · 0  | 0      | 0      |
|                        | 30 ppm     | 0     | 0           | 0        | 0      | 0    | Ő      | 0      | 0<br>0 | 0<br>0 | 0    | 0    | 0    | 0      | 0      |
| BNORMAL RESPIRA. SOUND | 0 ppm      | 0     | 0           | 0        | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      |
|                        | 3 ppm      | 0     | 0           | 0        | 0      | 0    | 0      | õ      | 0      | Ő      | 0    | 0    | 0    | 0      | 0      |
|                        | 10 ppm     | 0     | 0           | 0        | 0      | 0    | Ő      | ő      | 0      | Ő      | 0    | 0    | 0    | 0      |        |
|                        | 30 ppm     | 0     | 0           | 0        | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0<br>0 |
| SUBNORMAL TEMP         | 0 ppm      | 0     | 0           | 0        | 0      | 0    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      |
|                        | 3 ppm      | 0     | 0           | 0        | Õ      | Õ    | ů<br>0 | ů<br>0 | 0      | 0      | 0    | 0    | 0    | 0      | 0      |
|                        | 10 ppm     | 0     | Õ           | Õ        | 0<br>0 | 0    | 0      | 0      | 0      | 0      | 0    | 0    |      | -      | 0      |
|                        | 30 ppm     | 0     | 0           | õ        | õ      | Ö    | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0<br>0 |

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CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

### SEX : MALE

PAGE : 36

| 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   |
|                         |            | 1      | 1          | 1       | 1    | 1      | 1      | 1        | 1    | 1        | 1      | 1    | 1      | 1      | 1      |
|                         |            |        |            |         |      |        |        |          |      |          |        |      |        |        |        |
| CRUSTA                  | 0 ppm      | 0      | 0          | 0       | 0    | 0      | 0      | 0        | 0    | 0        | 0      | 0    | 0      | 0      | 0      |
|                         | 3 ppm      | 0      | 0          | 0       | 0    | 0      | 0      | 0        | 0    | 0        | 0      | 0    | 0      | 0      | 0      |
|                         | 10 ppm     | 0      | 0          | 0       | 0    | 0      | 0      | 0        | 0    | 0        | 0      | 0    | 0      | 0      | 0      |
|                         | 30 ppm     | 0      | 0          | 0       | 0    | 0      | 0      | 0        | 0    | 0        | 0      | 0    | 0      | 0      | 0      |
| ORTICOLLIS              | 0 ppm      | 0      | 0          | 0       | 0    | 0      | 0      | 0        | 0    | 0        | 0      | 0    | 0      | 0      | 0      |
|                         | 3 ppm      | 0      | 0          | 0       | 0    | 0      | 0      | 0        | 0    | 0        | õ      | Õ    | Õ      | Ő      | 0      |
|                         | 10 ppm     | 0      | 0          | 0       | 0    | 0      | 0      | 0        | õ    | 0        | õ      | õ    | 0      | 0      | 0      |
|                         | 30 ppm     | 0      | 0          | 0       | 0    | 0      | 0      | 0<br>0   | Ő    | 0        | 0      | 0    | 0      | 0      | 0      |
| IRREGULAR BREATHING     | 0 ppm      | 0      | 0          | 0       | 0    | 0      | 0      | 0        | 0    | 0        | 0      | 0    | 0      | 0      | 0      |
|                         | 3 ppm      | 0      | Ō          | 0       | õ    | õ      | 0      | 0        | 0    | 0        | 0      | 0    | -      |        | 0      |
|                         | 10 ppm     | 0      | 0          | Õ       | õ    | õ      | ŏ      | 0        | 0    | 0        | 0      | 0    | 0      | 0      | 0      |
|                         | 30 ppm     | 0      | 0          | 0       | 0    | 0      | 0      | 0        | 0    | 0        | 0      | 0    | 0<br>0 | 0<br>0 | 0<br>0 |
| BRADYPNEA               | 0 ppm      | 0      | 0          | 0       | 0    | 0      | 0      | 0        | 0    | <u>^</u> | 0      |      |        |        |        |
|                         | 3 ppm      | Ő      | õ          | õ       | 0    | 0      | . 0    | 0        | 0 -  | 0        | 0      | 0    | 0      | 0      | 0      |
|                         | 10 ppm     | 0      | 0          | Õ       | 0    | Ő      | 0      | 0        | 0    |          | -      | 0    | 0      | 0      | 0      |
|                         | 30 ppm     | Ő      | 0          | 0       | 0    | 0      | 0      | 0        | 0    | 0<br>0   | 0<br>0 | 0    | 0<br>0 | 0      | 0      |
| SHALLOW BREATHING       | 0 ppm      | 0      | 0          | 0       | 0    | ^      | 0      | <u>^</u> | •    |          | _      |      |        |        |        |
|                         | 3 ppm      | 0      | 0          | 0       | 0    | 0      | 0      | 0        | 0    | 0        | 0      | 0    | 0      | 0      | 0      |
|                         | 10 ppm     | 0      | 0          | 0       | 0    | 0      | 0      | 0        | 0    | 0        | 0      | 0    | 0      | 0      | 0      |
|                         | 30 ppm     | 0      | 0          | 0       | 0    | 0<br>0 | 0<br>0 | 0<br>0   | 0    | 0        | 0      | 0    | 0      | 0      | 0      |
|                         | oo bbm     | v      | v          | v       | U    | U      | U      | U        | 0    | 0        | 0      | 0    | 0      | 0      | 0      |
| ABNORMAL RESPIRA. SOUND | 0 ppm      | 0      | 0          | 0       | 0    | 0      | 0      | 0        | 0    | 0        | 0      | 0    | 0      | 0      | 0      |
|                         | 3 ppm      | 0      | 0          | 0       | 0    | 0      | 0      | 0        | 0    | 0        | 0      | Õ    | 0<br>0 | õ      | õ      |
|                         | 10 ppm     | 0      | 0          | 0       | 0    | 0      | 0      | 0        | 0    | Ő        | õ      | Ő    | 0      | 0<br>0 | 0      |
|                         | 30 ppm     | 0      | 0          | 0       | 0    | 0      | 0      | 0        | 0    | 0        | Ő      | 0    | 0      | 0      | 0      |
| SUBNORMAL TEMP          | 0 ppm      | 0      | 0          | 0       | 0    | 0      | 0      | 0        | 0    | 0        | 0      | 0    | 0      | 0      | 0      |
|                         | 3 ppm      | 0      | 0          | 0       | Õ    | õ      | 0<br>0 | 0        | õ    | ŏ        | 0      | 0    | 0      |        | 0      |
|                         | 10 ppm     | 0      | 0          | 0       | · 0  | õ      | õ      | 0        | 0    | 0        | 0      | 0    | 0      | 0<br>0 | 0      |
|                         | - 30 ppm   | 0      | 0          | 0       | 0    | õ      | õ      | Ő        | 0    | 0        | 0      | 0    | 0      | 0      | 0<br>0 |

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CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

(HAN190)

BAIS 3

### SEX : MALE

PAGE : 37

| Clinical sign          | Group Name | Admin  | istration 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   |
|                        |            | 1      | 1           | 1       | 1    | 1      | 1    | 1    | 1    | 1      | 1      | 1          | 1    | 1        | 1      |
|                        |            |        |             |         |      |        |      |      |      |        |        |            |      |          |        |
| CRUSTA                 | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0          | 0    | 0        | 0      |
|                        | 3 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0          | 0    | 0        | 0      |
|                        | 10 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0          | 0    | 0        | 0      |
|                        | 30 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0          | 0    | 0        | 0      |
| TORTICOLLIS            | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0          | 0    | 0        | 0      |
|                        | 3 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0          | 0    | 0        | 0      |
|                        | 10 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0          | Õ    | Õ        | Ő      |
|                        | 30 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0          | 0    | 0        | õ      |
| IRREGULAR BREATHING    | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | . 0  | 0      | 0      | 0          | 0    | 0        | 0      |
|                        | 3 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0      | 0      | õ          | 0    | Õ        | 0      |
|                        | 10 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | Õ      | Õ      | Ő          | Ő    | Õ        | Ő      |
|                        | 30 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0      | 0<br>0 | Ő          | 0    | 0        | 0      |
| BRADYPNEA              | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0          | 0    | 0        | 0      |
|                        | 3 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | Õ    | õ    | Ő      | õ      | 0          | 0    | 0        | 0      |
|                        | 10 ppm     | 0      | 0           | 0       | 0    | Õ      | Ő    | 0    | õ    | 0      | 0      | 0          | 0    | -        |        |
|                        | 30 ppm     | 0      | 0           | 0       | 0    | 0      | Õ    | 0    | 0    | õ      | 0<br>0 | 0          | 0    | 0<br>0   | 0<br>0 |
| SHALLOW BREATHING      | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0          | 0    | 0        | 0      |
|                        | 3 ppm      | 0      | 0           | 0       | Ō    | Õ      | Ő    | Õ    | õ    | 0<br>0 | 0      | 0          | 0    | 0        | -      |
|                        | 10 ppm     | Õ      | Ő           | õ       | Õ    | Ő      | ŏ    | 0    | 0    | 0      | 0      | 0          | 0    | 0        | 0<br>0 |
|                        | 30 ppm     | 0      | 0           | 0       | Ő    | õ      | Ő    | 0    | 0    | 0      | 0      | 0          | 0    | 0        | 0      |
| BNORMAL RESPIRA. SOUND | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0          | 0    | 0        | 0      |
|                        | 3 ppm      | 0      | 0           | Õ       | Õ    | ů<br>0 | 0    | 0    | 0    | 0      | 0      | 0          | 0    | 0        | 0      |
|                        | 10 ppm     | Ō      | Õ           | õ       | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0          | -    |          | 0      |
|                        | 30 ppm     | 0      | 0<br>0      | õ       | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0          | 0    | 0<br>0   | 0<br>0 |
| UBNORMAL TEMP          | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0      | 0      | <i>,</i> 0 | 0    | <u>^</u> | •      |
|                        | 3 ppm      | ů<br>0 | 0           | Ő       | 0    | 0      | 0    | 0    | 0    | 0<br>0 | 0      | 0          | 0    | 0        | 0      |
|                        | 10 ppm     | ů<br>0 | 0           | õ       | 0    | 0      | 0    | 0    | 0    |        |        | -          | 0    | 0        | 0      |
|                        | 30 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0      | 0      | 0          | 0    | 0        | 0      |
|                        | oo ppm     | v      | v           | v       | 0    | v      | U    | U    | U    | 0      | 0      | 0          | 0    | 0        | 0      |

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CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : MALE

PAGE : 38

| Clinical sign          | Group Name | Admini | stration W | eek-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     |
|                        |            | 1      | 1          | 1       | 1    | 1    | 1    | 1      | 1      | 1                                     | 1      | 1      | 1      | 1        | 1        |
|                        |            |        |            |         |      |      |      |        |        | · · · · · · · · · · · · · · · · · · · |        |        |        |          |          |
| CRUSTA                 | 0 ppm      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0      | 0                                     | 0      | 0      | 0      | 0        | 0        |
|                        | 3 ppm      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0      | õ                                     | Ő      | 0      | 0<br>0 | 0        | 0        |
|                        | 10 ppm     | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0      | Ő                                     | õ      | õ      | õ      | 0        | 0        |
|                        | 30 ppm     | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0      | 0                                     | Ő      | 0<br>0 | 0      | 0        | 0        |
| ORTICOLLIS             | 0 ppm      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0      | 0                                     | 0      | 0      | 0      | 0        | 0        |
|                        | 3 ppm      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | õ      | ů                                     | Ő      | 0      | 0      | 0        | 0        |
|                        | 10 ppm     | 0      | 0          | 0       | 0    | 0    | õ    | Õ      | 0      | ŏ                                     | 0      | 0      | 0      | -        |          |
|                        | . 30 ppm   | 0      | 0          | 0       | 0    | Ö    | 0    | 0      | 0      | 0                                     | 0      | 0      | 0      | 0<br>0   | 0        |
| IRREGULAR BREATHING    | 0 ppm      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0      | 0                                     | 0      | 0      | 0      | <u>^</u> | •        |
|                        | 3 ppm      | õ      | õ          | 0       | 0    | 0    | 0    | 0      | 0      | 0                                     | 0      | 0      | 0      | 0        | 0        |
|                        | 10 ppm     | õ      | Ő          | 0       | 0    | 0    | 0    | 0      | 0      | 0                                     | v      | 0      | 0      | 0        | 0        |
|                        | 30 ppm     | 0      | õ          | 0       | 0    | 0    | 0    | 0      | 0      | 0<br>1                                | 0<br>1 | 0<br>0 | 1<br>1 | 1<br>0   | 0<br>1   |
| BRADYPNEA              | 0 ppm      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0      |                                       |        |        | -      |          | -        |
|                        | 3 ppm      | õ      | 0<br>0     | 0       | 0    | 0    | 0    | 0      | 0<br>0 | 0                                     | 0      | 0      | 0      | 0        | 0        |
|                        | 10 ppm     | õ      | õ          | 0       | 0    | 0    | 0    | 0      |        | 0                                     | 0      | 0      | 0      | 0        | 0        |
|                        | 30 ppm     | 0      | Ő          | 0       | 0    | 0    | 0    | 0      | 0<br>0 | 0<br>0                                | 0      | 0<br>0 | 0<br>0 | 0        | 0<br>0   |
| HALLOW BREATHING       | mqq 0      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | •      |                                       |        | -      |        | -        |          |
|                        | 3 ppm      | õ      | 0          | 0       | 0    | 0    | 0    | 0      | 0      | 0                                     | 0      | 1      | 0      | 0        | 0        |
|                        | 10 ppm     | õ      | 0          | 0       | 0    | 0    | 0    | •      | 0      | 0                                     | 0      | 0      | 0      | 0        | 0        |
|                        | 30 ppm     | 0<br>0 | Ő          | 0       | 0    | 0    | 0    | 0<br>0 | 0<br>0 | 0<br>0                                | 0      | 0      | 0      | 0        | 0        |
|                        | pput       | č      | v          | v       | v    | v    | v    | U      | U      | U                                     | U      | 0      | 0      | 0        | 0        |
| BNORMAL RESPIRA. SOUND | 0 ppm      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0      | 0                                     | 0      | 0      | 0      | 0        | 0        |
|                        | 3 ppm      | 0      | 0          | 0       | 0    | õ    | õ    | 0      | 0      | 0                                     | 0      | 0      | 0      | 0        | 0        |
|                        | 10 ppm     | 0      | 0          | 0       | 0    | õ    | Ő    | 0<br>0 | 0      | 1                                     | 0      | 0      | 0      | 0        | 0<br>0   |
|                        | 30 ppm     | 0      | 0          | 0       | 0    | õ    | 0    | 0      | 1      | 1                                     | 1      | 0      | 0      | 0        | 0        |
| UBNORMAL TEMP          | 0 ppm      | 0      | 0          | 0       | 0    | 0    | 0    | 0      | 0      | 0                                     | 0      |        | 0      | <u>^</u> | <u>^</u> |
|                        | 3 ppm      | 0      | Ō          | õ       | 0    | õ    | 0    | 0      | 0      | 0                                     | 0      | 1<br>0 | 0      | 0        | 0        |
|                        | 10 ppm     | 0      | õ          | 0       | 0    | 0    | 0    | 0      | 0      | 0                                     | 0      | 0      | 0      | 0        | 0        |
|                        | 30 ppm     | 0      | õ          | õ       | 0    | 0    | 0    | 0      | 0      | 0                                     | 0      | 0      | 0<br>1 | 0        | 0<br>0   |

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### SEX : MALE

PAGE : 39

| Clinical sign          | Group Name | Admini | stration N | /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   |
|                        |            | 1      | 1          | 1        | 1    | 1    | 1    | 1    | 1    | 1    | 1      | 1    | 1      | 1        | 1      |
| THICT I                |            |        |            |          |      |      |      |      |      |      |        |      |        | ·        |        |
| CRUSTA                 | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0      |
|                        | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0        | Õ      |
|                        | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | Ő        | õ      |
|                        | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | Ō      | 0        | õ      |
| ORTICOLLIS             | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    |        | <u>,</u> |        |
|                        | 3 ppm      | 0      | 0          | 0        | 0    | õ    | Ő    | 0    | 0    | 0    | 0      | 0    | 1      | 0        | 0      |
|                        | 10 ppm     | 0      | 0          | õ        | Ő    | 0    | 0    | 0    | 1    | -    | 0      | 0    | 0      | 0        | 0      |
|                        | 30 ppm     | Õ      | ů          | 0        | 0    | 0    | 0    | 0    | 1    | 0    | 0      | 0    | 0      | 0        | 0      |
|                        | •••        |        | -          | Ť        | v    | v    | v    | v    | U    | U    | U      | 0    | 0      | 0        | 0      |
| RREGULAR BREATHING     | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0      |
|                        | 3 ppm      | 0      | 0          | 0        | 0    | 0    | õ    | õ    | 0    | 0    | 0      | 0    | 0      | 0        | 0      |
|                        | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 1    | Ő    | 0      | 0    | 1      | 0<br>1   | 0      |
|                        | 30 ppm     | 0      | 0          | 0        | 0    | 2    | 1    | Õ    | Ō    | 1    | 1      | 0    | 0      | 0        | 0<br>4 |
| RADYPNEA               | <b>A</b> . | •      |            |          |      |      |      |      |      |      |        |      | 0      | v        | 7      |
| NUD II NEA             | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0      |
|                        | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 1      | 0        | 0      |
|                        | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0      |
|                        | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 1      | 0    | 0      | 0        | 1      |
| HALLOW BREATHING       | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | •    |      |        | _    |        |          |        |
|                        | 3 ppm      | õ      | õ          | Õ        | õ    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0      |
|                        | 10 ppm     | Ő      | ů<br>0     | õ        | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0      |
|                        | 30 ppm     | Ő      | õ          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0      |
|                        |            |        | -          | ·        | •    | v    | v    | U    | U    | U    | 0      | 0    | 0      | 0        | 0      |
| BNORMAL RESPIRA. SOUND | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0      |
|                        | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | ů    | õ    | õ    | 0      | 0    | 0      | 0        | 0      |
|                        | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | õ    | õ    | Ő    | 0<br>0 | 0    | 0      | 0        | 0      |
|                        | 30 ppm     | 0      | 0          | 0        | 0    | 1    | 1    | Õ    | õ    | 2    | 2      | 2    | 0<br>2 | 1        | 0<br>2 |
| UBNORMAL TEMP          | 0          | •      | •          |          |      |      |      |      |      |      |        | -    | -      | •        | 0      |
| CDITOROAD I DRIF       | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0      |
|                        | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0,       | Ō      |
|                        | 10 ppm     | 0      | 1          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 1        | 0      |
|                        | 30 ppm     | 0      | 0          | 0        | 0    | 2    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 2      |

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CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : MALE

Clinical sign	Group Name	Admin	istration	Week-day				PAGE : 40
		99-7	100-7	101-7	102-7	103-7	104-7	
		1	1	1	1	1	1	
CRUSTA	0 ppm	0	0	0	0	0	٥	
	3 ppm	0	0	õ	1	1	0	
	10 ppm	0	Õ	Ő	0	0	1	
	30 ppm	Õ	Ő	0	0	0	0 0	
TORTICOLLIS						·	0	
IONTICOLLIS	0 ppm	0	0	0	0	0	0	
	3 ppm	0	0	0	0	0	0	
	10 ppm	0	0	1	0	0	0	
	30 ppm	0	0	0	0	0	0	
IRREGULAR BREATHING	0 ppm	0	0	0	•	•	_	
	3 ppm	0	0		0	0	0	
	10 ppm	0 0	0	0	0	0	0	
	30 ppm	2	3	1 4	0 7	0 6	0	
	••	-	v	т	1	0	8	
BRADYPNEA	0 ppm	0	0	0	0	0	0	
	3 ppm	0	0	Ō	õ	0	0	
	10 ppm	0	0	Ō	0	õ	0	
	30 ppm	0	0	Ő	1	0	1	
SHALLOW BREATHING	<u>^</u>						-	
JEIDEOR BREATHING	nqq 0	0	0	0	0	0	0	
	3 ppm	0	0	0	0	0	0	
	10 ppm	0	0	0	0	0	0	
	30 ppm	0	0	0	0	0	0	
ABNORMAL RESPIRA. SOUND	0 ppm	0	0					
	3 ppm	0		0	0	0	0	
	10 ppm	0	0	0	0	0	0	
	30 ppm	1	0 4	0	0	0	0	
	oo ppu	1	4	4	7	6	9	
SUBNORMAL TEMP	0 ppm	0	0	0	0	0	0	
	3 ppm	õ	0	0	0		0	
	10 ppm	Ő	0	0	0	0	0	
	30 ppm	õ	õ	1	0	0 0	0	
	P.P.M	v	v	1	v	U	0	

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PAGE : 40

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APPENDIX A 2

# CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(2-YEAR STUDY)

### SEX : FEMALE

PAGE : 41

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
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
ЕАТН	0	0	0	<u>^</u>	0	•				_	_				
DEATH	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ORIBUND SACRIFICE	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
OCOMOTOR MOVEMENT DECR	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	Õ	0 0	0	õ	ů 0	0	Ő	0	0
	10 ppm	Ő	0	Ő	Ő	õ	ŏ	0	0 0	0	0	0	0	0	0
	30 ppm	õ	0	0	Ő	ő	Ő	0	0	0	0	0	0	0	0 0
ATERAL	mqq 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	-			-	0	0	0	0
							-	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	U	0	0	0	0	0	0	0	0	0	0	0	0
UNCHBACK POSITION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ARALYTIC GAIT	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	õ	0	Ö	0	õ	0
ASTING	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	Ō	0	õ	0 0	õ	Ő	ů 0	0	0	0	ŏ	0
	10 ppm	õ	Õ	õ	Ő	Ő	0	0	0	0	0	0	0	0	0
	30 ppm	ő	0	õ	0	0	0	0	0	0	0	0	0	· 0	0
OILED	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	õ	õ	õ	0	0	0	0	0	0	0	0	0	0	
	10 ppm	õ	õ	õ	0	0	0	0	0	0	0	0			0
	30 ppm	õ	0	õ	0	0	0	0	0	0	0	0	0	0	0
	50 ppm	v	v	v	v	U	v	0	v	v	U	0	U	0	0

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CLINICAL OBSERVATION (SUMMARY)

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

### SEX : FEMALE

PAGE : 42

| 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 |
|                        | <u> </u>   | 1      | 1           | 1       | 1        | 1    | 1        | 1        | 1    | 1        | 1    | 1    | 1      | 1      | 1    |
| ЕАТН                   | 0          | 0      | 0           | 0       | •        |      | <u>^</u> | <u>^</u> |      | <u>^</u> |      |      |        |        |      |
| JEAIN                  | 0 ppm      | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | . 0  | 0    | 0      | 0      | 0    |
|                        | 3 ppm      | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |
|                        | 10 ppm     | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |
|                        | 30 ppm     | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |
| ORIBUND SACRIFICE      | mqq 0      | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |
|                        | 3 ppm      | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |
|                        | 10 ppm     | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |
|                        | 30 ppm     | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |
| OCOMOTOR MOVEMENT DECR | 0 ppm      | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |
|                        | 3 ppm      | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |
|                        | 10 ppm     | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |
|                        | 30 ppm     | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |
| ATERAL                 | 0 ppm      | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |
|                        | 3 ppm      | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | Ō      | 0    |
|                        | 10 ppm     | 0      | 0           | 0       | 0        | Ō    | 0        | Ő        | õ    | 0        | 0    | Õ    | ů<br>0 | Ő      | Õ    |
|                        | 30 ppm     | 0      | 0           | 0       | 0        | 0    | 0        | Õ        | 0    | 0        | õ    | õ    | õ      | Ő      | Ő    |
| UNCHBACK POSITION      | 0 ppm      | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |
|                        | 3 ppm      | 0      | 0           | Ō       | 0        | 0    | Ő        | Ő        | Ō    | 0        | Ő    | õ    | ů<br>0 | Ő      | õ    |
|                        | 10 ppm     | 0      | Ō           | Õ       | Ō        | Ő    | ů.       | Ő        | õ    | õ        | Ő    | ŏ    | Ő      | ů<br>0 | õ    |
|                        | 30 ppm     | 0      | 0           | 0       | Õ        | Ő    | Ő        | 0        | Ő    | õ        | Ő    | 0    | ů<br>0 | Ő      | 0    |
| ARALYTIC GAIT          | 0 ppm      | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |
|                        | 3 ppm      | 0      | 0           | 0       | 0        | 0    | 0        | Ő        | õ    | Ő        | õ    | õ    | õ      | Ő      | Ő    |
|                        | 10 ppm     | Ő      | õ           | Ő       | õ        | Ő    | 0        | ů<br>0   | 0    | õ        | 0    | ŏ    | 0      | 0      | 0    |
|                        | 30 ppm     | 0      | õ           | ů<br>0  | 0        | õ    | 0        | õ        | õ    | 0        | 0    | 0    | 0      | õ      | 0    |
| AŞTING                 | 0 ppm      | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |
| •                      | 3 ppm      | õ      | ů<br>0      | 0       | õ        | 0    | 0        | õ        | 0    | õ        | 0    | 0    | 0      | 0      | 0    |
|                        | 10 ppm     | õ      | ŏ           | 0       | 0<br>0   | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |
|                        | 30 ppm     | õ      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |
|                        | 0.5        | 0      | 0           | 0       | <u>^</u> |      | 0        |          |      |          |      |      |        |        |      |
| SOILED                 | 0 ppm      | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |
|                        | 3 ppm      | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |
|                        | 10 ppm     | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |
|                        | 30 ppm     | 0      | 0           | 0       | 0        | 0    | 0        | 0        | 0    | 0        | 0    | 0    | 0      | 0      | 0    |

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

### SEX : FEMALE

PAGE : 43

| Clinical sign           | Group Name | Admini   | 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     | 40-7   | 41-7 | 42-7 |
|                         |            | 1        | 1          | 1       | 1        | 1    | 1    | 1        | 1        | 1    | 1        | 1        | 1      | 1    | 1    |
| 17 1 TT 1               |            | <u>^</u> | <u>^</u>   | 0       | <u>,</u> | 0    | 0    | <u>^</u> | <u>^</u> |      | <u>^</u> | <u>,</u> |        | 0    |      |
| DEATH                   | 0 ppm      | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         | 3 ppm      | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         | 10 ppm     | 0<br>0   | 0<br>0     | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0<br>0   | 0        | 0<br>0 | 0    | 0    |
|                         | 30 ppm     | U        | U          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | U        | U        | U      | U    | 0    |
| IORIBUND SACRIFICE      | O ppm      | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         | 3 ppm      | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         | 10 ppm     | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         | 30 ppm     | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
| LOCOMOTOR MOVEMENT DECR | 0 ppm      | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         | 3 ppm      | Ő        | Õ          | Ő       | õ        | Ő    | õ    | õ        | Õ        | 0    | 0        | Ő        | Õ      | 0    | õ    |
|                         | 10 ppm     | 0        | õ          | õ       | õ        | 0    | 0    | Ő        | ő        | õ    | 0        | 0        | 0      | 0    | 0    |
|                         | 30 ppm     | ů<br>0   | Ő          | 0<br>0  | ů        | Ő    | 0    | õ        | õ        | õ    | õ        | õ        | Ő      | õ    | 0    |
|                         | ppul       | -        | ÷          | -       | •        | -    |      | -        | ÷        |      | -        |          | -      | ÷    | -    |
| LATERAL                 | 0 ppm      | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         | 3 ppm      | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         | 10 ppm     | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         | 30 ppm     | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
| HUNCHBACK POSITION      | 0 ppm      | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         | 3 ppm      | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | Ó    | 0        | 0        | 0      | 0    | 0    |
|                         | 10 ppm     | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         | 30 ppm     | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
| PARALYTIC GAIT          | 0 ppm      | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         | 3 ppm      | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         | 10 ppm     | 0        | 0          | õ       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         | 30 ppm     | 0        | 0          | 0       | 0        | õ    | Ő    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         |            |          |            |         |          |      |      |          |          |      |          |          |        |      |      |
| WASTING                 | 0 ppm      | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         | 3 ppm      | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         | 10 ppm     | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         | 30 ppm     | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
| SOILED                  | 0 ppm      | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         | 3 ppm      | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         | 10 ppm     | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |
|                         | 30 ppm     | 0        | 0          | 0       | 0        | 0    | 0    | 0        | 0        | 0    | 0        | 0        | 0      | 0    | 0    |

### SEX : FEMALE

PAGE : 44

| linical sign           | Group Name |        | istration W |      |      |        |      |          |      |      |        |        |        |        |        |
|------------------------|------------|--------|-------------|------|------|--------|------|----------|------|------|--------|--------|--------|--------|--------|
|                        |            | 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   |
|                        |            | 1      | 1           |      | 1    | 1      | 1    |          | 1    | 1    | 1      | 1      | 1      | 1      | 1      |
| ЕАТН                   | 0          | 0      |             | 0    | 0    |        |      | <u>^</u> |      |      |        |        |        |        | _      |
| EAIN                   | 0 ppm      | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
|                        | 3 ppm      | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
|                        | 10 ppm     | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
|                        | 30 ppm     | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
| ORIBUND SACRIFICE      | 0 ppm      | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
|                        | 3 ppm      | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
|                        | 10 ppm     | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
|                        | 30 ppm     | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
| DCOMOTOR MOVEMENT DECR | 0 ppm      | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
|                        | 3 ppm      | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
|                        | 10 ppm     | Õ      | õ           | Õ    | 0    | Ő      | Ő    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
|                        | 30 ppm     | 0      | õ           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
|                        | oo ppiii   | v      | v           | v    | v    | v      | v    | U        | v    | v    | U      | v      | U      | v      | 0      |
| ATERAL                 | 0 ppm      | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
|                        | 3 ppm      | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
|                        | 10 ppm     | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
|                        | 30 ppm     | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
| JNCHBACK POSITION      | 0 ppm      | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
|                        | 3 ppm      | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
|                        | 10 ppm     | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
|                        | 30 ppm     | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | õ      | 0      | õ      | Õ      |
| ARALYTIC GAIT          | 0 ppm      | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | ^      | 0      |
|                        | 3 ppm      | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0<br>0 | 0<br>0 | 0<br>0 | 0      |
|                        | 10 ppm     | 0      | 0           | 0    | 0    | 0      | 0    | 0        |      |      |        |        |        |        | 0      |
|                        | 30 ppm     | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0<br>0 |
|                        | an hhu     | U      | U           | U    | U    | U      | U    | U        | U    | U    | U      | U      | U      | U      | U      |
| ASTING                 | 0 ppm      | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
|                        | 3 ppm      | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
|                        | 10 ppm     | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
|                        | 30 ppm     | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
| OILED                  | 0 ppm      | 0      | 0           | 0    | 0    | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      | 0      | 0      |
|                        | 3 ppm      | 0      | 0           | 0    | 0    | 0      | Õ    | õ        | Õ    | õ    | õ      | 0<br>0 | Ő      | 0      | 0      |
|                        | 10 ppm     | 0      | 0           | 0    | 0    | Ő      | Õ    | Õ        | Ő    | ŏ    | õ      | õ      | Ő      | Õ      | 0      |
|                        | 30 ppm     | 0<br>0 | 0           | 0    | 0    | ů<br>0 | Ő    | Õ        | 0    | Õ    | 0<br>0 | õ      | 0      | ŏ      | ŏ      |

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CLINICAL OBSERVATION (SUMMARY)

### SEX : FEMALE

PAGE : 45

| 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   |
|                         |            | 1      | 1          | 1       | 1    | 1      | 1    | 1      | 1      | 1      | 1      | 1      | 1      | 1      | 1      |
| EATH                    | 0          | 0      | 0          | 0       | 0    | 0      |      |        |        |        |        |        | _      |        |        |
| JEATH                   | 0 ppm      | 0      | 0          | 0       | 0    | 0      | 1    | 1      | 1      | 1      | 1      | 1      | 1      | 1      | 2      |
|                         | 3 ppm      | 0      | 0          | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                         | 10 ppm     | 0      | 0          | 0       | 1    | 1      | 1    | 1      | 1      | 1      | 1      | 1      | 1      | 1      | 1      |
|                         | 30 ppm     | 0      | 0          | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| MORIBUND SACRIFICE      | 0 ppm      | 0      | 0          | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                         | 3 ppm      | 0      | 0          | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                         | 10 ppm     | 0      | 0          | 0       | 0    | 1      | 1    | 1      | 1      | 1      | 1      | 1      | 1      | 1      | 1      |
|                         | 30 ppm     | 0      | 0          | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| LOCOMOTOR MOVEMENT DECR | 0 ppm      | 0      | 0          | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                         | 3 ppm      | 0      | 0          | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                         | 10 ppm     | 0      | 0          | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                         | 30 ppm     | 0      | 0          | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| ATERAL                  | 0 ppm      | 0      | 0          | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                         | 3 ppm      | 0      | 0          | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0<br>0 |
|                         | 10 ppm     | 0      | 0          | 0       | 0    | 0      | 0    | 0      | 0      | 0      | Ō      | 0      | Ő      | õ      | Õ      |
|                         | 30 ppm     | 0      | 0          | 0       | 0    | 0      | 0    | 0      | õ      | õ      | ŏ      | õ      | 0<br>0 | 0      | 0      |
| FUNCHBAGK POSITION      | 0 ppm      | 0      | 0          | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                         | 3 ppm      | 0      | 0          | 0       | 0    | Ō      | 0    | 0      | Ō      | õ      | Ő      | 0<br>0 | 0<br>0 | ů      | 0      |
|                         | 10 ppm     | 0      | 0          | Ō       | 0    | õ      | õ    | Ő      | õ      | 0      | 0      | 0      | 0      | 0      | 0<br>0 |
|                         | 30 ppm     | 0      | 0          | 0       | 0    | Ő      | Ő    | 0<br>0 | Ő      | 0<br>0 | 0<br>0 | 0 .    | 0      | 0      | 0      |
| PARALYTIC GAIT          | mqq 0      | 0      | 0          | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 1      | 1      | 0      |
|                         | 3 ppm      | 0      | 0          | Ő       | õ    | Ő      | õ    | Õ      | 0<br>0 | Õ      | Ő      | 0      | 0      | 0      | 0      |
|                         | 10 ppm     | 0      | Ő          | Õ       | õ    | ů<br>0 | õ    | ů<br>0 | 0      | 0      | õ      | 0      | 0      | 0<br>0 | 0      |
|                         | 30 ppm     | Ő      | õ          | õ       | 0    | õ      | õ    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| #ASTING                 | 0 ppm      | 0      | 0          | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                         | 3 ppm      | 0      | 0          | 0       | 0    | 0      | 0    | Õ      | Õ      | 0      | õ      | õ      | Õ      | Ő      | ŏ      |
|                         | 10 ppm     | Õ      | 0          | õ       | õ    | Ő      | õ    | ů<br>0 | 0      | Ő      | 0      | 0      | 0      | 0      | 0      |
|                         | 30 ppm     | 0      | 0          | 0       | 0    | 0      | 0    | Ő      | 0      | Ő      | 0      | 0      | 0      | Õ      | 0      |
| SOILED                  | 0 ppm      | 0      | 0          | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                         | 3 ppm      | 0      | 0          | 0       | 0    | 0      | Ō    | Ő      | õ      | õ      | õ      | Ő      | Ö      | 0      | 0      |
|                         | 10 ppm     | 0      | 0          | 0       | Ō    | Ō      | õ    | Ő      | õ      | ŏ      | ŏ      | õ      | 0      | Ő      | 0      |
|                         | 30 ppm     | 0      | 0          | 0       | 0    | 0      | õ    | ů<br>0 | õ      | õ      | õ      | õ      | Ő      | 0      | 0      |

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CLINICAL OBSERVATION (SUMMARY)

### SEX : FEMALE

PAGE : 46

| linical sign           | Group Name | Admini | stration W |        | · · · · · · · · · · · · · · · · · · · |      |      |      |        |      |      |        |        |        |        |
|------------------------|------------|--------|------------|--------|---------------------------------------|------|------|------|--------|------|------|--------|--------|--------|--------|
|                        |            | 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   |
|                        |            | 1      | 1          | 1      | 1                                     | 1    | 1    | 1    | 1      | 1    | 1    | 1      | 1      | 1      | 1      |
| EATH                   | 0 ppm      | 2      | 9          | 0      | 0                                     | 2    | 0    | 0    |        | 0    |      | 2      |        |        |        |
| DAIII                  | 3 ppm      | 0      | 2<br>0     | 2<br>0 | 3                                     | 3    | 3    | 3    | 3      | 3    | 3    | 3      | 4      | 4      | 4      |
|                        |            |        |            |        | 1                                     | 1    | 1    | 1    | 1      | 2    | 2    | 2      | 2      | 2      | 2      |
|                        | 10 ppm     | 1      | 1          | 1      | 1                                     | 1    | 1    | 1    | 1      | 1    | 1    | 1      | 1      | 1      | 1      |
|                        | 30 ppm     | 0      | 0          | 1      | 1                                     | 1    | 1    | 1    | 1      | 2    | 2    | 2      | 3      | 3      | 3      |
| DRIBUND SACRIFICE      | 0 ppm      | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      |
|                        | 3 ppm      | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      |
|                        | 10 ppm     | 1      | 1          | 1      | 1                                     | 1    | 1    | 1    | 1      | 1    | 1    | 1      | 1      | 1      | 1      |
|                        | 30 ppm     | 0      | 0          | 0      | 0                                     | 0    | 0    | 2    | 2      | 2    | 2    | 2      | 2      | 2      | 2      |
| DCOMOTOR MOVEMENT DECR | 0 ppm      | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      |
|                        | 3 ppm      | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      |
|                        | 10 ppm     | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      |
|                        | 30 ppm     | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      |
| TERAL                  | 0 ppm      | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | 0    | 0    | 0      | `<br>0 | 0      | 0      |
|                        | 3 ppm      | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      |
|                        | 10 ppm     | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | . 0    |
|                        | 30 ppm     | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      |
| JNCHBACK POSITION      | nqq 0      | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | 0    | 0    | 0 -    | 0      | 0      | 0      |
|                        | 3 ppm      | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | 0    | 0    | 0<br>0 | 0      | 0      | õ      |
|                        | 10 ppm     | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | 0    | 0    | 0      | Ő      | Ő      | Õ      |
|                        | 30 ppm     | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | 0    | 1    | 1      | 0      | Ő      | ů<br>0 |
| ARALYTIC GAIT          | 0 ppm      | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      |
|                        | 3 ppm      | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | ů<br>0 | Õ      |
|                        | 10 ppm     | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | Õ      | Õ    | 0    | õ      | 0      | õ      | õ      |
|                        | 30 ppm     | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | 0    | õ    | õ      | 0      | õ      | ů<br>0 |
| ASTING                 | 0 ppm      | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      |
|                        | 3 ppm      | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | Ő    | Õ    | õ      | Õ      | Õ      | Ő      |
|                        | 10 ppm     | 0      | 0          | 0      | 0                                     | 0    | Ō    | Ő    | õ      | Ő    | õ    | ŏ      | 0      | 0      | õ      |
|                        | 30 ppm     | 0      | 0          | 0      | 0                                     | 0    | 0    | Õ    | õ      | õ    | 0    | 0      | 0<br>0 | Ő      | 0      |
| OILED                  | 0 ppm      | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      |
|                        | 3 ppm      | 0      | 0          | 0      | 0                                     | 0    | 0    | 0    | 0      | 0    | 0    | õ      | Ő      | Ő      | õ      |
|                        | 10 ppm     | 0      | 0          | 0      | 0                                     | 0    | Ō    | Õ    | 0<br>0 | õ    | Õ    | Ő      | õ      | 0      | 0      |
|                        | 30 ppm     | 0      | 0          | 0      | 0                                     | 0    | Õ    | 0    | õ      | õ    | Õ    | Ő      | 0      | 0      | ő      |

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

### SEX : FEMALE

PAGE : 47

linical sign	Group Name		istration W												
		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
		1	1	1	1	1	1	1	1	1.	1	1	1	1	1
EATH	0 ppm	4	4	4	4	4	4	4	4	1	4	5	5	6	7
<i>0</i> /111 <i>3</i>	3 ppm	2	2	2	2	4	6	6	6	6	7	7	8	10	10
	10 ppm	1	1	1	1	1	1	1	1	1	I	1	1	10	2
	30 ppm	3	3	3	4	4	4	4	4	4	4	5	5	5	6
ORIBUND SACRIFICE	0 ppm	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	3 ppm	0	0	0	0	0	1	1	1	ĩ	2	2	2	2	2
	10 ppm	1	1	1	3	3	3	3	3	3	3	3	4	4	4
	30 mag	2	2	3	3	3	3	3	4	6	6	6	8	8	10
OCOMOTOR MOVEMENT DECR	0 ppm	0	0	0	0	1	0	0	0	С	0	0	0	0	0
	3 ppm	0	0	0	0	0	1	0	0	С	1	0	0	0	0
	10 ppm	0	0	0	1	0	0	0	0	С	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	1	1	0	0	2	0	1
ATERAL	0 ppm	0	0	0	0	0	0	0	0	С	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	С	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	1	0	0	0	0	0
UNCHBACK POSITION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	. 0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ррш	0	1	0	0	0	0	0	0	0	0	0	0	0	0
PARALYTIC GAIT	0 ppm	0	0	0	0	0	0	0	0	C	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm 30 ppm	0 0	0 0	0 0	0 0	0	0	0	0	0 0	0	0	0	0	0 0
ASTING		0	0	0	0		0		0						
1401 110	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	L	0	0	0	0	0	0	0	0	0	0	0	1
OILED	0 ppm 3 ppm	0 0	0 0	0 0	0 0	0	0 0	0	0	0	0	0	0	0	0
	3 ppm 10 ppm	0	0	0	0	0 0	0	0 0	0 0	0	0	0	0	0	0
		0	0	0	0	0	0	U 1	1	0	0	0	0	0	0
	30 ppm	U	U	U	U	U	U	1	1	0	0	0	0	0	0

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CLINICAL OBSERVATION (SUMMARY)

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : FEMALE

PAGE : 48

Clinical sign	Group Name	Admin	istration	¥eek-dav						 
-	•	99-7	100-7	101-7	102-7	103-7	104-7			
	· · · · · · · · · · · · · · · · · · ·	1	1	1	1	1	1	 	 	
DEATH	0 ppm	7	7	7	7	7	7			
	3 ppm	10	10	10	10	10	10			
	10 ppm	2	3	3	3	3	3			
	30 ppm	6	6	6	6	6	6			
MORIBUND SACRIFICE	0 ppm	2	2	2	2	2	2			
	3 ppm	2	2	2	2	2	2			
	10 ppm	5	6	6	7	7	7			
	30 ppm	10	11	11	11	12	12			
LOCOMOTOR MOVEMENT DECR	0 ppm	0	0	0	0	0	0			
	3 ppm	0	0	0	0	0	0			
	10 ppm	1	1	0	1	0	0			
	30 ppm	0	1	0	0	1	0			
LATERAL	0 ppm	0	0	0	0	0	0			
	3 ppm	0	0	0	0	0	0			
	10 ppm	0	0	0	0	0	0			
	30 ppm	0	0	0	0	0	Ő			
HUNCHBACK POSITION	0 ppm	0	0	0	0	0	0			
	3 ppm	0	0	0	0	0	0			
	10 ppm	0	0	0	0	0	0			
	30 ppm	0	0	0	Ő	0	Ő			
PARALYTIC GAIT	0 ppm	0	0	0	0	0	0			
	3 ppm	0	0	0	0	0	0			
	10 ppm	0	0	Ő	Õ	ů 0	Ő			
	30 ppm	õ	õ	õ	õ	o	õ			
WASTING	0 ppm	0	0	0	0	0	0			
	3 ppm	0	0	0	Ō	Ō	õ			
	10 ppm	Ő	õ	0 0	1	Ő	0			
	30 ppm	0 0	Õ	Ő	0	0	0			
									1	
SOILED	0 ppm	0	0	0	0	0	0			
	3 ppm	0	0	0	0	0	0			
	10 ppm	0	0	0	1	0	0			
	30 ppm	0	0	0	0	0	0			

## ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

### SEX : FEMALE

PAGE: 49

															PAGE · 4
Clinical sign	Group Name	Admini	stration W	eek-day		• • • • • • • • • • • • • • • • • • • •									
		1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7	14-7
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
PILOERECTION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
FROG BELLY	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SOILED PERI GENITALIA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EXOPHTHALMOS	0 ppm	0	0	0	0	0	0	1	1	1	1	1	1	1	1
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	1	1	1	1	1
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CATARACT	0 ppm	0	0	0	0	0	0	0	0	0	1	1	1	1	1
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CORNEAL OPACITY	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ANTERIOS CHAMBER OPACITY	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
INTERNAL MASS	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

STUDY NO. : 0342

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

SEX : FEMALE

PAGE : 50

Clinical sign	Group Name	Admini	stration 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
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
PILOERECTION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
FROG BELLY	mqq 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	. 0	0	0	0	0
SOILED PERI GENITALIA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EXOPHTHALMOS	mqq 0	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CATARACT	0 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	3 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	10 ppm	0	0	0	0	0	0	0	0	0	1	1	1	1	1
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CORNEAL OPACITY	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	<sup>′</sup> 0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	. 0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ANTERIOS CHAMBER OPACITY	0 ppm	0	0	1	1	1	1	1	1	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
INTERNAL MASS	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

### SEX : FEMALE

PAGE : 51

linical sign	Group Name		istration W								•				
		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
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
ILOERECTION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
TEGEREOITON	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ROG BELLY	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	õ	0	Õ	0 ·	õ	ů	Õ	õ	õ	Ő	Õ	õ	Ő
	30 ppm	0 0	0 T	õ	0	0	õ	õ	õ	0	õ	õ	õ	õ	Ő
OILED PERI GENITALIA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
XOPHTHALMOS	0 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ATARACT	0 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	3 ppm	1	1	1	2	2	2	2	2	2	2	2	2	2	2
	10 ppm	1	1	2	2	2	2	2	2	2	2	2	2	2	2
	30 ppm	. 0	0	0	0	0	0	0	0	0	0	0	0	0	0
CORNEAL OPACITY	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
NTERIOS CHAMBER OPACITY	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
NTERNAL MASS	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 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

PAGE : 52

Clinical sign	Group Name	Admini	istration 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
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
	\$														
PILOERECTION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ō	0
	10 ppm	0	0	0	0	0	0	0	Ō	0	õ	0	Õ	Ö	· 0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ROG BELLY	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	õ	õ	0	0
	10 ppm	0	Õ	Õ	õ	Ŏ	ů 0	Õ	õ	Õ	õ	õ	õ	Ő	0 0
	30 ppm	ő	0	0	0	0	0	0	õ	0	0	0	0	õ	0
SOILED PERI GENITALIA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	Ő	Õ	õ	õ	õ	ů 0	Ő	õ	0	0	0	õ	ő
	10 ppm	õ	ŏ	ŏ	ŏ	Ő	0 0	Õ	0 0	õ	õ	0 0	0 0	õ	0
	30 ppm	Ő	Õ	0 0	0	0	õ	Ő	õ	õ	õ	õ	0	0	0 0
XOPHTHALMOS	0 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	3 ppm	Ô	Ô	Ô	Ô	Ô	Ô	Ô	Ô	Ô	Ô	Ô	0	0	0 0
	10 ppm	ĩ	1	ĩ	1	ů 1	1	1	1	1	1	1	1	1	1
	30 ppm	0	0	0	0	0	0	0	Ô	0	0	0	0	0	0
ATARACT	0 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	3 ppm	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	10 ppm	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	30 ppm	0	Ō	0	0	õ	0	0	0	0	0	0	0	õ	0
CORNEAL OPACITY	maga O	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	Ō	Ō	0	0	0	Ő	0 0
	10 ppm	0	0	Ő	0	0 0	Õ	Ő	õ	Õ	Õ	õ	Õ	Õ	ŏ
	30 ppm	õ	õ	õ	õ	ő	ő	õ	0	0 0	õ	0	o	õ	0
ANTERIOS CHAMBER OPACITY	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	Ô	Ő	ŏ	Õ	Ő	õ
	10 ppm	0	0	0	0	0	0	0	0	Õ	Ő	õ	Ő	Ő	Ő
	30 ppm	0	õ	0	0	õ	0	Ő	õ	Ő	0	0	Ő	0 0	0
INTERNAL MASS	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	Ō	Ő	Ō	0	Ō	Ō
	30 ppm	0	0	0	0	0	0	0	0 0	0	0	õ	0	0	Ő

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CLINICAL OBSERVATION (SUMMARY)

### SEX : FEMALE

PAGE : 53

Clinical sign	Group Name	Admini	istration 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
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
PILOERECTION	0 ppm	0	0	0	0	0	0	0	0	· 0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ō	Ō
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ROG BELLY	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ō	Ő
	30 ppm	0	0	0	0	0	0	0	0	0	õ	õ	õ	õ	0
SOILED PERI GENITALIA	0 ppm	0	0	0	0	0	0	0	0	0	1	0	1	1	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ō	0
	10 ppm	0	0	0	0	0	0	0	0	0 0	Ő	õ	0 0	õ	ŏ
	30 ppm	0	0	0	0	0	0	0	0	0	ů.	Ő	0	ů 0	Ő
XOPHTHALMOS	0 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	3 ppm	0	0	0	0	0	Ô	Õ	ô	Ô	0	0	0	0	0
	10 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	30 ppm	0	0	ō	0	ō	ō	Ô	Ô	Ô	0	0	0	0	1
CATARACT	0 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	3 ppm	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	10 ppm	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CORNEAL OPACITY	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	õ	0	Ő	Ő	Ő	0	0	0
	10 ppm	0	0	0	0	õ	õ	Ő	0	0	0	0	0	0	0
	30 ppm	0	Ő	õ	0	õ	0	0	0	0	0	0	0	0	0
NTERIOS CHAMBER OPACITY	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	Ō	Õ	Ő	õ	0	0	0	0	0	0	0	0
	10 ppm	õ	Õ	õ	0 0	0	Ő	0	0	0	0	0	0	0	0
	30 ppm	0	0	õ	0 0	0 0	Ő	0	0	0	0	0	0	0	0
INTERNAL MASS	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	Ō	Ö	ů 0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	õ	0 0	õ	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	Õ	0	ů 0	0	õ	õ	0	0	0	0	0

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CLINICAL OBSERVATION (SUMMARY)

### SEX : FEMALE

PAGE : 54

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Clinical sign	Group Name		istration W												
		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
		1		1	1	1	1	1	1	1	1	1	1	1	1
LOERECTION	<u>,</u>	0							-	_	_				
ILUERECTION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	1	1	1	1	1	1
ROG BELLY	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0 .	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	30 ppm	0	1	0	0	0	0	0	0	0	0	. 1	0	0	0
DILED PERI GENITALIA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
IOPHTHALMOS	0 ppm	1	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	1	1	1	1	1	1	1	1	1	1	1	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	Ō	0	0	0	0	0
ATARACT	0 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	3 ppm	2	2	2	2	2	2	2	2	2	2	2	$\hat{2}$	2	2
	10 ppm	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	30 ppm	0	0	0	0	0	0	0	0	0	Ő	0	0	0	0
DRNEAL OPACITY	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	õ	Õ	0	ů	ů	0 0	õ	0	0	0	0	0
	10 ppm	Ő	Ő	Õ	õ	0	Ő	0	Ő	0	ŏ	0	0	0	0
	30 ppm	Ő	õ	õ	õ	0	õ	0	õ	õ	0 0	õ	0	0	0
TERIOS CHAMBER OPACITY	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	õ	0	0 0	0	0	0	ŏ	0	0	0	0	0	0
	10 ppm	Ő	Ő	0 0	õ	0	0	0	0	0	0	0	0	0	0
	30 ppm	Ő	0	0 0	0	0	0	0	0	0	0	0	0	0	0
NTERNAL MASS	0 ppm	0	1	1	1	1	1	1	1	1	1	1	1	1	1
	3 ppm	0	0	0	0 0	0	0	0	0	0	0	0	0	0	0
	10 ppm	õ	0 0	0	0	0	0 0	0	0	0	0	0	0	0	1
	30 ppm	0 0	õ	0	Ő	Ő	0	0	0	1	1	1	0	0	0

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CLINICAL OBSERVATION (SUMMARY)

### SEX : FEMALE

(HAN190)

PAGE : 55

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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
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
	<u>,</u>	•		•			_		_						
PILOERECTION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	1	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	1	1	0	0	0	0	0	0	0	0	0	0	0	0
FROG BELLY	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	1	1	1	1	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	1	0	0	0	0
SOILED PERI GENITALIA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	1	1	1	0	0	0	Õ	Ő	õ	Õ	ů 0	1	0
	30 ppm	0	0	1	0	0	Ő	1	1	1	1	õ	1	0	1
XOPHTHALMOS	mqq 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	Ő	Ő	ŏ	ŏ	õ	õ	0	0 0	Ő
	10 ppm	0	õ	õ	õ	0	õ	0 0	Ő	0	õ	0	0	Ő	0
	30 ppm	ŏ	0	õ	0	õ	0	0	0	0	0	0	0	0	0
ATARACT	0 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	2
	3 ppm	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	10 ppm	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	30 ppm	0	0	0	0	0	õ	0	0	0	0	0	0	0	0
CORNEAL OPACITY	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	Ő	0	0	0	0	0	0	0	0	0	0	-		0
	10 ppm	0	0	0				-	-		-	-	0	0	0
		0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	U	U	U	0	0	0	0	0	0	0	0	0	0	0
INTERIOS CHAMBER OPACITY	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
INTERNAL MASS	0 ppm	1	1	1	2	1	1	1	1	· 1	1	0	0	0	0
	3 ppm	0	0	1	1	0	0	0	0	0	0	0	0	0	0
	10 ppm	1	1	1	1	0	0	0	0	0	1	1	0	1	2
	30 ppm	0	0	1	0	0	0	0	0	0.	1	0	0	. 0	0

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CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

### SEX : FEMALE

PAGE : 56

Clinical sign	Group Name	Admini	stration	Week-day _				 	 	
-	-	99-7	100-7	101-7	102-7	103-7	104-7			
		1	1	1	1	1	1			
ILOERECTION	0 ppm	0	0	0	0	0	0			
	3 ppm	0	0	0	0	0	0			
	10 ppm	0	0	0	0	0	0			
	30 ppm	0	0	0	0	0	0			
FROG BELLY	0 ppm	0	0	0	0	0	0			
	3 ppm	0	0	0	0	0	0			
	10 ppm	0	0	0	0	0	0			
	30 ppm	0	0	0	0	0	0			
SOILED PERI GENITALIA	0 ppm	1	1	1	1	1	1			
	3 ppm	0	0	0	0	Ō	1			
	10 ppm	1	Õ	õ	õ	Ő	ō			•
	30 ppm	õ	0	0	0	1	0			
EXOPHTHALMOS	0 ppm	0	0	0	0	0	0			
	3 ppm	Ō	0	0	0	0	Ō			
	10 ppm	Õ	õ	Ő	ů 0	Ő	0			
	30 ppm	Ő	0	õ	õ	0	õ			
CATARACT	0 ppm	2	3	. 3	3	3	3			
	3 ppm	2	2	2	2	2	2			
	10 ppm	2	2	2	2	2	2			
	30 ppm	0	Ō	0	0	õ	0			
CORNEAL OPACITY	0 ppm	0	0	0	0	0	1			
	3 ppm	õ	ů	õ	õ	Ő	0			
	10 ppm	Õ	0	0	0	0	0			
	30 ppm	0	0	0	0	0	0			
ANTERIOS CHAMBER OPACITY	0 ppm	0	0	0	0	0	0			
	3 ppm	0	0	Õ	Ő	0	Õ			
	10 ppm	õ	Ő	Õ	Ő	Ő	Ő			
	30 ppm	Ő	0	0	0	0	0			
INTERNAL MASS	mqq 0	0	0	0	0	0	0			
	3 ppm	0	0	0	1	1	2			
	10 ppm	2	3	2	2	1	2			
	30 ppm	Ő	Õ	1	2	2	3			

CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

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### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

SEX : FEMALE

PAGE : 57

| 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   |
|                       |            | 1      | 1           | 1      | 1      | 1      | 1      | 1   | 1      | 1   | 1    | 1      | 1    | 1    | 1      |
| . NOSE                | mag O      | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0      |
| . NUOL                |            | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0<br>0 | 0   | 0    | 0<br>0 | 0    | 0    | 0      |
|                       | 3 ppm      |        |             |        |        |        | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0      |
|                       | 10 ppm     | 0      | 0           | 0      | 0<br>0 | 0      |        | 0.  | 0      | 0   | 0    | 0      | 0    | 0    | 0      |
|                       | 30 ppm     | 0      | 0           | 0      | U      | 0      | 0      | U   | U      | U   | 0    | U      | U    | U    | U      |
| . EYE                 | 0 ppm      | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0      |
|                       | 3 ppm      | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0      |
|                       | 10 ppm     | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0      |
|                       | 30 ppm     | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0      |
| .PERI MOUTH           | 0 ppm      | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0      |
|                       | 3 ppm      | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0      |
|                       | 10 ppm     | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0      |
|                       | 30 ppm     | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0      |
| ORAL CAVITY           | 0 ppm      | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0      |
|                       | 3 ppm      | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0      |
|                       | 10 ppm     | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0      |
|                       | 30 ppm     | 0      | õ           | õ      | õ      | 0      | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0      |
| I. MANDIBULAR         | 0 ppm      | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0      |
|                       | 3 ppm      | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0      |
|                       | 10 ppm     | ŏ      | õ           | Ő      | Õ      | Ő      | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0      |
|                       | 30 ppm     | 0      | 0<br>0      | 0      | Ő      | 0      | 0      | 0   | õ      | 0   | 0    | 0      | 0    | 0    | 0      |
| I. EAR                | 0 ppm      | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0      |
|                       | 3 ppm      | õ      | 0           | Õ      | 0      | 0      | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0      |
|                       | 10 ppm     | Ő      | õ           | õ      | õ      | Ő      | Ő      | Õ   | Õ      | 0   | 0    | 0      | 0    | 0    | 0      |
|                       | 30 ppm     | õ      | 0           | 0      | 0      | õ      | õ      | 0   | 0      | õ   | 0    | Ő      | 0    | 0    | 0      |
| I. PERI EAR           | 0 ppm      | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0      | 0   | . 0  | 0      | 0    | 0    | 0      |
| and the second second | 3 ppm      | Ő      | õ           | Õ      | Ő      | 0<br>0 | õ      | Õ   | õ      | Ő   | 0    | 0      | 0    | 0    | 0      |
|                       | 10 ppm     | Ő      | 0<br>0      | 0      | 0<br>0 | 0      | Ő      | Ő   | ŏ      | ŏ   | õ    | õ      | Õ    | Ő    | Õ      |
|                       | 30 ppm     | õ      | 0           | 0      | 0      | 0      | 0<br>0 | Õ   | ° 0    | Ő   | õ    | õ      | 0    | Õ    | 0      |
|                       | so ppm     | v      | v           | v      | U      | v      | v      | Ū   | v      | v   | v    | v      | v    | v    | v      |
| l HEAD                | 0 ppm      | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0<br>0 |
|                       | 3 ppm      | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0      | 0   | 0    |        | 0    |      |        |
|                       | 10 ppm     | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0      | 0   | 0    | 0      | -    | 0    | 0      |
|                       | 30 ppm     | 0      | 0           | 0      | 0      | 0      | 0      | 0   | 0      | 0   | 0    | 0      | 0    | 0    | 0      |

### SEX : FEMALE

PAGE : 58

| Clinical sign  | Group Name | Admini | stration W | Veek-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 |
|                |            | 1      | 1          | 1        | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                |            |        |            |          |      |      | _    | _    |      |      |      |      |      |      |      |
| M. NOSE        | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. EYE         | 0 ppm      | 0      | 0          | 0        | . 0  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI MOUTH  | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ORAL CAVITY | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. MANDIBULAR  | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. EAR         | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR    | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. HEAD        | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 10 ppm     | 0      | 0          | 0        | . 0  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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CLINICAL OBSERVATION (SUMMARY)

### SEX : FEMALE

PAGE : 59

| Clinical sign  | Group Name | Admini | istration 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 | 40-7 | 41-7   | 42-7   |
|                |            | 1      | 1           | 1       | 1    | 1      | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1      | 1      |
| 1. NOSE        | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 3 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    |        | 0      |
|                | 10 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0<br>0 | 0      |
|                | 30 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0<br>0 |
| I. EYE         | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 3 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 10 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 30 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
| M. PERI MOUTH  | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 3 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 10 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 30 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
| M. ORAL CAVITY | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 3 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 10 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 30 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
| M. MANDIBULAR  | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 3 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 10 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 30 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
| M. EAR         | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 3 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 10 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 30 ppm     | 0      | U           | U       | 0    | 0      | 0    | 0    | 0    | . 0  | 0    | 0    | 0    | 0      | 0      |
| M.PERI EAR     | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 3 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 10 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 30 ppm     | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
| M. HEAD        | 0 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 3 ppm      | 0      | 0           | 0       | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 10 ppm     | 0      | 0           | 0       | 0    | 0<br>0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                | 30 ppm     | U      | U           | U       | U    | U      | υ    | U    | U    | U    | 0    | U    | 0    | 0      | 0      |

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CLINICAL OBSERVATION (SUMMARY)

### SEX : FEMALE

PAGE : 60

| Clinical sign                         | Group Name |      | istration W |      |      |      |      |      |      |      |      |      |      |      |      |
|---------------------------------------|------------|------|-------------|------|------|------|------|------|------|------|------|------|------|------|------|
|                                       |            | 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 |
| · · · · · · · · · · · · · · · · · · · |            | 1    | 1           | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                                       |            |      |             |      |      |      |      |      |      |      | •    |      |      |      |      |
| 1. NOSE                               | 0 ppm      | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | Ò    | 0    | 0    |
|                                       | 3 ppm      | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 10 ppm     | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 30 ppm     | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| I. EYE                                | 0 ppm      | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 3 ppm      | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 10 ppm     | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 30 ppm     | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| 4. PERI MOUTH                         | 0 ppm      | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 3 ppm      | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 10 ppm     | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 30 ppm     | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| I ORAL CAVITY                         | 0 ppm      | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 3 ppm      | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 10 ppm     | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 30 ppm     | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| 4. MANDIBULAR                         | 0 ppm      | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 3 ppm      | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 10 ppm     | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 30 ppm     | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. EAR                                | 0 ppm      | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 3 ppm      | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 10 ppm     | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 30 ppm     | 0    | 0           | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| M. PERI EAR                           | 0 ppm      | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 3 ppm      | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 10 ppm     | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 30 ppm     | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| 4. HEAD                               | 0 ppm      | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 3 ppm      | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 10 ppm     | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                                       | 30 ppm     | 0    | 0           | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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CLINICAL OBSERVATION (SUMMARY)

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CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

### SEX : FEMALE

PAGE : 61

| linical sign  | Group Name     | Admini | istration 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   |
|               |                | 1      | 1           | 1       | 1    | 1    | 1    | 1      | 1    | 1      | 1      | 1      | 1                                       | 1      | 1      |
| I. NOSE       | 0              | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |
| I. NUSE       | 0 ppm          | 0      | 0           | 0       | 0    |      | 0    | -      | 0    | 0      | 0      | -      | 0                                       | -      | 0      |
|               | 3 ppm          |        | 0           | 0       | 0    | 0    | 0    | 0      | 0    | •      | 0      | 0<br>0 | 0<br>0                                  | 0      | 0      |
|               | 10 ppm         | 0<br>0 | 0           | 0       | 0    | 0    | 0    | 0<br>0 | 0    | 0<br>0 | 0<br>0 | 0      | 0                                       | 0<br>0 | 0<br>0 |
|               | 30 ppm         | U      | U           | U       | U    | U    | U    | U      | U    | U      | U      | U      | U                                       | U      | U      |
| l eye         | 0 ppm          | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |
|               | 3 ppm          | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |
|               | 10 ppm         | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |
|               | 30 ppm         | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |
| 4. PERI MOUTH | 0 ppm          | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |
|               | 3 ppm          | 0      | 0           | õ       | Õ    | 0    | õ    | 0      | õ    | 0      | ů<br>0 | Õ      | 0                                       | Õ      | Ő      |
|               | 10 ppm         | 0      | 0           | Ō       | 0    | Ō    | Ō    | 0      | 0    | Õ      | Õ      | Ō      | Ő                                       | õ      | 0      |
|               | 30 ppm         | 0      | 0.          | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |
| . ORAL CAVITY | 0              | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | •      |        |
| LORAL CAVIII  | 0 ppm<br>3 ppm | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0<br>0 | 0<br>0 |
|               | 10 ppm         | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |
|               | 30 ppm         | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |
|               | oo ppm         | U      | Ŷ           | 0       | Ū    | U    | v    | 0      | U    | U      | U      | U      | U                                       | U      | 0      |
| A. MANDIBULAR | 0 ppm          | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |
|               | 3 ppm          | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |
|               | 10 ppm         | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |
|               | 30 ppm         | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |
| I. EAR        | 0 ppm          | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |
|               | 3 ppm          | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | Ő      | 0                                       | 0      | 0      |
|               | 10 ppm         | 0      | 0           | 0       | 0    | Ō    | 0    | 0      | 0    | Õ      | Õ      | õ      | Õ                                       | Ő      | õ      |
|               | 30 ppm         | 1      | 1           | 1       | 1    | 1    | 1    | 1      | 1    | 1      | 1      | 1      | 1                                       | 1      | 1      |
| M. PERI EAR   | 0 ppm          | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |
|               | 3 ppm          | 0      | ő           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |
|               | 10 ppm         | 1      | 1           | 1       | 1    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |
|               | 30 ppm         | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |
|               | oo huu         | v      | v           | v       | v    | v    | v    | v      | v    | v      | v      | v      | v                                       | v      | U      |
| M. HEAD       | mqq 0          | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 1      |
|               | 3 ppm          | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |
|               | 10 ppm         | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |
|               | 30 ppm         | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0                                       | 0      | 0      |

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### SEX : FEMALE

PAGE : 62

| Clinical sign  | Group Name       | Admini | istration N | /eek-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    |
|                |                  | 1      | 1           | 1        | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1       |
| 1. NOSE        | 0 ppm            | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | D    | 0    | 0       |
| . NOOL         | 3 ppm            | 0      | 0           | 0        | 0    | 0    |      | 0    | 0    | 0    |      |      |      | 0    |         |
|                |                  | 0      |             |          |      | -    | 0    |      |      |      | 0    | 0    | 0    |      | 0       |
|                | 10 ppm           |        | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       |
|                | 30 ppm           | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       |
| 1. EYE         | 0 ppm            | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       |
|                | 3 ppm            | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       |
|                | 10 ppm           | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       |
|                | 30 ppm           | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       |
| 1. PERI MOUTH  | 0 ppm            | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       |
|                | andd S           | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0.   | 0    | 0    | 0       |
|                | 10 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    |      |         |
|                | 30 ppm           | U      | U           | U        | U    | U    | U    | U    | U    | U    | U    | U    | U    | 0    | 0       |
| I. ORAL CAVITY | 0 ppm            | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       |
|                | 3 ppm            | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       |
|                | 10 ppm           | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       |
|                | 30 ppm           | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       |
| I. MANDIBULAR  | 0 ppm            | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       |
|                | 3 ppm            | 0      | 0           | 0        | 0    | 0    | Õ    | Ő    | 0    | 0    | õ    | õ    | õ    | Õ    | õ       |
|                | 10 ppm           | 0      | 0           | Ő        | 0    | Ō    | Ő    | 0    | 0    | Ő    | Ő    | Ő    | 0    | Ő    | 0       |
|                | 30 ppm           | Ő      | Õ           | Ő        | Õ    | ŏ    | ů    | 0    | 0    | õ    | 0    | Ő    | 0    | õ    | 0       |
|                | oo ppin          | 0      | v           | Ū        | 0    | v    | v    | U    | v    | v    | v    | v    | U    | v    | U       |
| 4. EAR         | 0 ppm            | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       |
|                | 3 ppm            | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       |
|                | 10 ppm           | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       |
|                | 30 ppm           | 1      | 1           | 1        | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1       |
| L PERI EAR     | 0 ppm            | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       |
|                | 3 ppm            | 0      | 0           | 0        | Ó    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | Ő       |
|                | 10 ppm           | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | ů    | õ    | 0<br>0  |
|                | 30 ppm           | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | Ő    | Ő    | õ    | 0    | Ő    | 0<br>0  |
| I. HEAD        | mqq 0            | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | .0      |
| *** *******    | 3 ррш            | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | .U<br>0 |
|                | 10 ppm           | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       |
|                | 10 ppm<br>30 ppm | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0       |
|                | 30 ppm           | U      | U           | U        | U    | υ    | U    | U    | U    | U    | U    | U    | U    | U    | U       |

CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

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### SEX : FEMALE

PAGE : 63

| 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 |
|               |            | 1      | 1          | 1       | 1    | 1    | 1      | 1      | 1      | 1      | 1      | 1    | 1      | 1    | 1    |
| NOSE          | 0 ppm      | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
| NUOL          |            | 0      | 0          | 0       | 0    |      |        |        | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
|               | 3 ppm      | 0      | -          | 0<br>1  |      | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
|               | 10 ppm     |        | 1<br>0     | 0       | 1    | 1    | 1      | 1      | 1      | 1      | 1      | 1    | 1      | 1    | 1    |
|               | 30 ppm     | 0      | U          | U       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
| EYE           | 0 ppm      | 1      | 1          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
|               | 3 ppm      | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
|               | 10 ppm     | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
|               | 30 ppm     | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
| .PERI MOUTH   | 0 ppm      | 1      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
|               | 3 ppm      | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
|               | 10 ppm     | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
|               | 30 ppm     | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
| ORAL CAVITY   | 0 ppm      | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
|               | 3 ppm      | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
|               | 10 ppm     | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
|               | 30 ppm     | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | Õ    | Ō      | Ō    | 0    |
| . MANDIBULAR  | 0 ppm      | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
|               | 3 ppm      | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | Õ    |
|               | 10 ppm     | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | Ō      | Ō    | 0      | õ    | ŏ    |
|               | 30 ppm     | 0      | 0          | 0       | 0    | 1    | 1      | 1      | 1      | 1      | 1      | 1    | ı<br>1 | 1    | 1    |
| I. EAR        | 0 ppm      | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
|               | 3 ppm      | õ      | õ          | 0       | ů    | Ő    | Õ      | 0      | 0<br>0 | 0      | 0<br>0 | Ő    | 0      | õ    | õ    |
|               | 10 ppm     | õ      | ů          | õ       | õ    | Ő    | 0<br>0 | 0<br>0 | 0      | 0<br>0 | 0      | 0    | 0      | Ő    | 0    |
|               | 30 ppm     | 1      | 1          | 1       | 1    | 1    | 1      | 1      | 1      | 1      | 1      | 1    | 1      | 1    | 0    |
| LPERI EAR     | 0 ppm      | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
| a tent thin   | maga 8     | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
|               | 10 ppm     | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
|               | 30 ppm     | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
|               | so ppm     | U      | U          | U       | U    | U    | U      | U      | U      | U      | v      | v    | U      | U    | U    |
| . HEAD        | 0 ppm      | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
|               | 3 ppm      | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
|               | 10 ppm     | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |
|               | 30 ppm     | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    |

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CLINICAL OBSERVATION (SUMMARY)

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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SEX : FEMALE

PAGE : 64

Clinical sign	Group Name	Admin	istration	Week-day _					
		99-7	100-7	101-7	102-7	103-7	104-7		
		1	1	1	1	1	1	 	
. NOSE	0 ppm	0	0	0	0	0	0		
	3 ppm	0	0	0	0	0	0		
	10 ppm	1	1	1	1	1	1		
	30 ppm	0	0	0	0	0	0		
. EYE	mqq 0	0	0	0	0	0	0		
	3 ppm	0	0	0	0	0	0		
	10 ppm	0	0	0	0	0	0		
	30 ppm	0	0	0	0	0	0		
A. PERI MOUTH	0 ppm	0	0	0	0	0	0		
	3 ppm	0	0	0	0	0	0		
	10 ppm	0	0	0	0	0	0		
	30 ppm	0	0	0	0	0	0		
A. ORAL CAVITY	0 ppm	0	0	0	0	0	0		
	3 ppm	0	0	0	0	0	0		
	10 ppm	0	0	0	0	0	0		
	30 ppm	0	0	1	1	1	1		
I. MANDIBULAR	0 ppm	0	0	0	0	0	0		
	3 ppm	0	0	0	0	0	0		
	10 ppm	0	0	0	0	0	0		
	30 ppm	1	1	1	1	1	1		
I. EAR	0 ppm	0	0	0	0	0	0		
	3 ppm	0	0	0	0	0	0		
	10 ppm	0	0	0	0	0	0		
	30 ppm	0	0	0	0	0	0		
I. PERI EAR	0 ppm	0	0	0	0	0	0		
	3 ppm	0	0	0	0	0	0		
	10 ppm	0	0	0	0	0	0		
	30 ppm	0	0	0	0	0	0		
I. HEAD	0 ppm	0	0	0	0	0	0		
	3 ppm	0	0	0	0	0	0		
	10 ppm	0	0	0	0	0	0		
	30 ppm	0	0	0	0	0	0		

### SEX : FEMALE

PAGE : 65

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
		1	1	1	1	1	1	. 1	1	1	1	1	1	1	1
M. NECK	0	0	0	0			<u>,</u>	•					_		_
I. NECK	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M. BREAST	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	Ő	ů	ů	Õ	ů	õ
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	ů	0	ů
M. ABDOMEN	mqq 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0 0	0	0	0	0	0	0	0		-	0		-	
	10 ppm	0	0	0	0	0				0	0	-	0	0	0
							• 0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
M. POSTERIOR DORSUM	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ő	0
M. GENITALIA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	õ	ů	õ	õ	Ő	õ	0 0	0	ŏ	0	0	0	0	0
	10 ppm	0	0	õ	õ	0	0	0	0	0		0	•		
	30 ppm	0	0	0	0	0					0		0	0	0
	30 ppm	U	U	U	0	U	0	0	0	0	0	0	0	0	0
ANEMIA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
JAUNDISE	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	õ	Õ	õ	õ	Ő	õ	õ	ŏ	Ő	0	0	0	0	0
	10 ppm	0	0	0	0	0	Õ	õ	õ	Ő	0	0	0	Ő	0
	30 ppm	0	õ	0	õ	0	0	0	0	õ	0	0	Ő	0	0
CRUSTA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0		-	-	0	0	0	0
	3 ppm 10 ppm	0	0	0	0	0			0	0	0	0	0	0	0
			0	0			0	0	0	0	0	0	0	0	0
	30 ppm	0	U	U	0	0	0	0	0	0	0	0	0	0	0

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CLINICAL OBSERVATION (SUMMARY)

#### SEX : FEMALE

PAGE : 66

Clinical sign	Group Name		istration 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
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
. NECK	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
. BREAST	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
I. ABDOMEN	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
L POSTERIOR DORSUM	0 ppm	0	0	0	0	. 0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A. GENITALIA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
NEMIA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
JAUNDISE	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CRUSTA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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CLINICAL OBSERVATION (SUMMARY)

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

#### SEX : FEMALE

PAGE : 67

| Clinical sign      | Group Name | Admini | 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   | 40-7 | 41-7   | 42-7   |
|                    |            | 1      | 1          | 1        | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1      | 1    | 1      | 1      |
| I. NECK            | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 3 ppm      | 0      | Ō          | 0        | õ    | Õ    | õ    | 0    | Õ    | õ    | õ    | 0<br>0 | õ    | õ      | ů<br>0 |
|                    | 10 ppm     | 0      | 0          | 0        | 0    | Ō    | 0    | 0    | Õ    | õ    | 0    | õ      | õ    | ů<br>0 | õ      |
|                    | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0.     | 0      |
| BREAST             | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 10 ppm     | 0      | 0          | 0        | o    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
| I. ABDOMEN         | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 3 ppm      | 0      | 0          | 0        | 0    | · 0  | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 10 ppm     | 0      | 0          | 0        | 0 -  | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
| . POSTERIOR DORSUM | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
| A. GENITALIA       | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0.     |
| ANEMIA             | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
| JAUNDISE           | 0 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
| CRUSTA             | mqq 0      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 3 ppm      | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 10 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |
|                    | 30 ppm     | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0      | 0      |

#### SEX : FEMALE

PAGE : 68

| 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   |
|                    |            | 1      | 1          | 1       | 1      | 1      | 1    | 1    | 1        | 1    | 1    | 1      | 1      | 1        | 1      |
| . NECK             | 0 ppm      | 0      | 0          | 0       | 0      | 0      | 0    | 0    | <u>^</u> |      | 0    | 0      | 0      | <u>,</u> | •      |
| . NECK             | 3 ppm      | 0      | 0          | 0       | 0<br>0 | 0<br>0 | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 10 ppm     | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0<br>0   | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 30 ppm     | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0<br>0 | 0<br>0 | 0<br>0   | 0<br>0 |
| I. BREAST          | 0 ppm      | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 3 ppm      | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 10 ppm     | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 30 ppm     | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
| 4. ABDOMEN         | 0 ppm      | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | . 0    |
|                    | 3 ppm      | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 10 ppm     | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 30 ppm     | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
| L POSTERIOR DORSUM | mqq 0      | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 3 ppm      | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 10 ppm     | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 30 ppm     | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
| A. GENITALIA       | mqq 0      | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 3 ppm      | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 10 ppm     | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 30 ppm     | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
| ANEMIA             | 0 ppm      | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 3 ppm      | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 10 ppm     | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 30 ppm     | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
| JAUNDISE           | 0 ppm      | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 3 ppm      | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 10 ppm     | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 30 ppm     | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
| CRUSTA             | 0 ppm      | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 3 ppm      | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 10 ppm     | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |
|                    | 30 ppm     | 0      | 0          | 0       | 0      | 0      | 0    | 0    | 0        | 0    | 0    | 0      | 0      | 0        | 0      |

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CLINICAL OBSERVATION (SUMMARY)

#### SEX : FEMALE

PAGE : 69

Clinical sign	Group Name	Admini	istration 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
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
I. NECK	0	0	<u>^</u>	0	<u>^</u>	<u>^</u>		<u>^</u>	<u>,</u>						
I. NEUR	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
I. BREAST	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
I. ABDOMEN	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	õ	0	õ	Õ	õ	ů	0	0	0 0	õ	0
	10 ppm	0	Ő	Ő	Ő	Ő	õ	õ	Ő	õ	0 0	0 0	0	Ő	0
	30 ppm	Ő	Õ	ő	õ	Ő	ŏ	0	0	Ő	0	0 0	0	0	0
A POSTERIOR DORSUM		^	•	-		-	_	-	_	_					
1. POSTERIOR DURSUM	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	1	1	1	1	1	1
A. GENITALIA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	• 0
ANEMIA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	Ō	õ	Ő	ů	ů 0	õ	õ	0 0	0	õ	0	0	õ	0
	10 ppm	ŏ	õ	0	Ő	0 0	0	0	Ő	Ő	0	0	0	0	0
	30 ppm	0	0	0 0	õ	0 0	0	0	0 0	õ	0	0	0	0	0
IAUNDISE	0	0	0	0	0	0	0	0	0	•	0	0	0	<u>,</u>	~
201010101010	0 ppm 3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm 10 ppm	0	0	0					-	0	0	0	0	0	0
		0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	U	U	U	0	U	0	0	0	0	0	0	0	0	0
CRUSTA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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CLINICAL OBSERVATION (SUMMARY)

#### SEX : FEMALE

PAGE : 70

Clinical sign	Group Name	Admini	stration W	eek-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
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
NECK	0 ppm	0	0	0	0	0	0		1				<u>^</u>	<u>^</u>	
NECK	3 ppm	0 0	0	0	0 0	0	0	1	1	1	1	1	0	0	0
				0		0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
. BREAST	0 ppm	0	0	0	0	0	0	0	0	0	1	1	1	1	1
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	10 ppm	0	0	0	0	0	0	0	1	1	1	1	1	1	2
	30 ppm	1	1	1	1	1	1	1	1	1	1	1	2	2	2
I. ABDOMEN	0 ppm	0	0	0	1	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	õ	Õ	Ô	õ	õ	Ő	0 0	õ	õ	0	0	0	0
	10 ppm	Ő	0	Õ	0	Ő	õ	0	0	Ő	Ő	0	0	0	0
	30 ppm	Ő	Ő	1	1	1	1	1	1	1	1	1	1	1	1
POSTERIOR DORSUM	0	0	^	•	0	•	<u>,</u>	•			•				
FOSTERIOR DORSOM	0 ppm	0 0	0	0	0	0	0	0 0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	-	0	0	0	0	0	0	0
	10 ppm 30 ppm	1	1	1	0 1	0 1	0 1	0	0	0	0	0	0	0	0
	30 ppm	1	1	1	I	1	1	1	1	1	1	1	1	1	1
. GENITALIA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
NEMIA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	Õ	õ	ů 0	0	Õ	õ	ů
	10 ppm	0	0	0	Ō	1	Õ	ů	Ő	Ő	0	Õ	Õ	Ő	0
	30 ppm	0	0	0	0	Ō	0	0 0	õ	õ	õ	ő	ő	õ	0
AUNDISE	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	٥	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0 0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0 0
DICT	•								_						
RUSTA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	U	U	U	1	1	1	1	1	1	1	1	1	1	1

CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

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#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

#### SEX : FEMALE

PAGE : 71

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
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
I. NECK	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
. BREAST	0 ppm	1	1	1	1	1	1	2	2	2	3	3	3	3	3
	mqq E	1	0	0	0	0	0	1	1	15	1	1	1	0	0
	10 ppm	2	3	3	2	1	1	1	2	2	2	3	4	4	5
	30 ppm	2	3	3	4	4	4	5	5	5	4	4	4	5	8
. ABDOMEN	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	3 ppm	0	0	0	1	1	1	1	1	1	1	2	2	1	1
	10 ppm	0	0	0	0	0	1	1	1	1	2	2	2	2	1
	30 ppm	1	1	1	1	1	1	1	1	2	2	2	2	4	3
. POSTERIOR DORSUM	mag 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	1	1	1	1	. 1	1	1	1	1	1	1	1	1	1
I. GENITALIA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	1	1	1	0	0	0	0	0
	10 ppm	0	0	1	1	1	1	1	1	1	1	1	1	1	2
	30 ppm	0	0	0	0	0	0	1	1	0	0	1	1	1	0
INEMIA	0 ppm	0	0	0	0	1	0	0	0	0	1	0	· 0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	1	1	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	1	1	0
AUNDISE	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	1
RUSTA	Ó ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	1	1	1	1	1	1	1	1	1	1	1	1	1	1

#### SEX : FEMALE

PAGE : 72

Clinical sign	Group Name	Admin	istration	Week-day _							
		99-7	100-7	101-7	102-7	103-7	104-7				
		1	1	1	1	1	1	 	 		
I. NECK	0 ppm	0	0	0	0	0	1				
- -	3 ppm	0	0	0	. 0	0	0				
	10 ppm	0	0	0	0	0	0				
	30 ppm	0	0	0	0	0	0				
M. BREAST	0 ppm	4	4	4	4	4	4				
	3 ppm	1	1	1	3	3	3				
	10 ppm	5	5	6	7	7	8				
	30 ppm	8	8	7	9	9	12				
M. ABDOMEN	0 ppm	1	2	2	2	2	3				
	3 ppm	1	2	2	2	2	2				
	10 ppm	1	2	. 3	5	5	5				
	30 ppm	3	3	3	3	3	6				
M. POSTERIOR DORSUM	0 ppm	0	0	0	0	0	0				
	3 ppm	0	0	0	0	0	0				
	10 ppm	0	0	0	0	0	0				
	30 ppm	1	1	1	1	1	1				
M. GENITALIA	0 ppm	0	0	0	0	0	0				
	3 ppm	0	0	0	0	0	0				
	10 ppm	2	1	1	1	1	1				
	30 ppm	0	0	0	0	0	0				
ANEMIA	0 ppm	0	0	0	0	0	0				
	3 ppm	0	0	0	0	0	0				
	10 ppm	0	1	0	0	0	0				
	30 ppm	0	1	0	0	1	1				
JAUNDISE	0 ppm	0	0	0	0	0	0				
	3 ppm	0	0	0	0	0	0				
	10 ppm	0	0	0	0	0	0				
	30 ppm	0	0	0	0	0	0				
CRUSTA	0 ppm	0	0	0	0	0	0				
	3 ppm	0	0	0	0	0	0				
	10 ppm	0	0	0	0	0	0				
	30 ppm	1	1	1	1	1	1				

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CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

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#### SEX : FEMALE

PAGE : 73

linical sign	Group Name		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
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
EMORRHAGE	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Edonicii 101	3 ppm	0	0	õ	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0 0	0 0	0	õ	õ	0	0	0	õ	0	0	0	0
	30 ppm	0	0 0	0	0	0	0	õ	0	0	õ	õ	0	o	0
RREGULAR BREATHING	mqq 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
RADYPNEA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EEP BREATHING	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
BNORMAL RESPIRA. SOUND	mqq 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
JENORMAL TEMP	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ALIVATION	mqq 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 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

PAGE : 74

Clinical sign	Group Name	Admini	stration 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
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
IEMORRHAGE	0 ppm	0	0	.0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
RREGULAR BREATHING	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
BRADYPNEA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DEEP BREATHING	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRA. SOUND	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SUBNORMAL TEMP	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SALIVATION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 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

PAGE : 75

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Clinical sign	Group Name		istration W				· · · · · · · · · · · · · · · · · · ·								
		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
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
IEMORRHAGE	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
INTOUR MOL	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	õ	0	Ő	0	0	0	0	0	0	0	0	0	0
	30 ppm	õ	õ	0	0	õ	0	0	0	0	0	0	0	0	0
RREGULAR BREATHING	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
BRADYPNEA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	. 0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DEEP BREATHING	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
BNORMAL RESPIRA. SOUND	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SUBNORMAL TEMP	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SALIVATION	0 ppm	0	0	0	0	0	0	. 0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 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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(HAN190)

#### SEX : FEMALE

PAGE : 76

Clinical sign	Group Name	Admin	istration 🛛												
		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
	·····	1	1	1	1	1	1	1	1	1	1	1	1	1	1
ENORRHAGE	0 ppm	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
REGULAR BREATHING	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ADYPNEA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EP BREATHING	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
BNORMAL RESPIRA. SOUND	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
JENORMAL TEMP	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
LIVATION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 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

PAGE : 77

Clinical sign	Group Name		istration P												
		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
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
HEMORRHAGE	0	0	0	0	0	0	0	0	0	0		0	0	0	0
IEMORICIAGE	0 ppm 3 ppm	0	0	0	0	0	0	0	-	0	0	0	0	0	0
			0	0	0.	0	0	-	0	0		0	-	0	0
	10 ppm	0	0	0	0			0	0	0	0	0	0	0	0
	30 ppm	0	U	U	0	0	0	0	0	0	0	0	0	0	0
RREGULAR BREATHING	0 ppm	0	0	0	0	0	0	0	0	0	0	. 0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
BRADYPNEA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DEEP BREATHING	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRA. SOUND	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	Ō	Õ	õ	Õ	Õ	0
	10 ppm	0	0	Ō	0	0	0	0	Ō	Ō	Ō	Ő	0	õ	Ō
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SUBNORMAL TEMP	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	Õ	Ő	õ	Õ	õ	Õ	õ	õ	Ő	õ	Ő	Õ	õ	0 0
	10 ppm	õ	õ	õ	õ	õ	õ	õ	õ	õ	õ	Ő	ŏ	õ	Õ
	30 ppm	õ	õ	õ	Ő	0	ů 0	Ő	õ	õ	0	õ	0	Ő	o
SALIVATION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0 0	0	õ	Ő	Ő	ŏ	0 0	Ő	0	0	Ő	0	ŏ	0
	10 ppm	0	0	ŏ	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	Ő	0	0	0	0	Ő	0	0	0	0	0	0	0	0

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CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

BAIS 3

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 104

SEX : FEMALE

PAGE : 78

linical sign	Group Name	Admini	istration W	eek-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
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
IEMORRHAGE	0	0	0	0	0	0	0	0	<u>^</u>	0	0	0	0	0	<u>^</u>
ISMOUNTAGE	0 ppm 3 ppm	0	0	0	0 0	0 0	0	0 0	0 0	0	0	0	0 0	0	0
	3 ppm 10 ppm	0	0	0	0		0			0	0	0	-	0	0
	30 ppm	0	0	0	0	1 0	0	0 0	0 0	0	0	0	0 0	0	0 0
	so hhu	0	v	U	U	U	U	U	U	U	0	U	U	U	U
RREGULAR BREATHING	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	2	2	2	0	0	0	0	0	0	0	0
BRADYPNEA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	Õ	õ	Ő	0 0	Ő	õ	0 0	Ő	õ
	10 ppm	0	Ő	Ō	Ō	ŏ	õ	õ	ů	Ő	ů 0	ů	Ő	õ	Ő
	30 ppm	0	0	0	0	0	0	0	0	0	Ő	0	Ő	Ő	0
DEEP BREATHING	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
JEL DIEATITING	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0 0
	10 ppm	0	0	0	0	0	0	0	0	-	0	0	-		
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0 0
	20 hhm	U	U	v	U	U	U	U	U	U	U	U	U	0	0
ABNORMAL RESPIRA. SOUND	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SUBNORMAL TEMP	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	Ō	Ō	Õ	Õ	õ	Ő	Õ	Õ	Ő	ŏ	Ő	õ	õ
	10 ppm	0	0	0	Ō	0	õ	Ő	Õ	ů	0	õ	Ő	õ	ů 0
	30 ppm	0	0	0	0	0	0	õ	0	0	ů 0	0	Ő	ů 0	ů
SALIVATION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	1	1	1	1	1

(HAN190)

BAIS 3

#### SEX : FEMALE

PAGE : 79

linical sign	Group Name	Admini	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
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
EMORRHAGE	<u>^</u>	•						_	_	_					
EMURRHAGE	0 ppm	0	0	0	0	0	0	0	0	0	1	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0		0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	1	0	0
REGULAR BREATHING	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	. 1	0	0	0	1	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ō	0
	30 ppm	0	0	0	0	0	0	0	1	1	0	0	2	0	0
RADYPNEA	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	. 0	õ	0	õ	õ	0	0	0	0	0	0
	10 ppm	Ő	Õ	Ő	0	0	0	0	0	Ő	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	Û	1	1	ů	Ő	Ő	Õ	Ő
EP BREATHING	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	Õ	õ	Ő	0	0	0 0	Ő	. 0	0	0	0	0	0
	10 ppm	Õ	Õ	õ	1	0	0	Ő	0	0	0	0	0	0	0
	30 ppm	õ	õ	õ	0	õ	0 0	0	0	0	0	0	0	0	0
NORMAL RESPIRA. SOUND	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	Ô	õ	õ	õ	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	Ő	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	ő	õ	0	0	0 0	0	0	1	0	0	0	0	0	0
BNORMAL TEMP	0 ppm	0	0	0	0	1	0	0	0	^	0	0	0	^	C
	3 ppm	0	0	0	0	0	0	0	. 0	0	0 1	0	0	0	0
	10 ppm	0	0	0	1	0	0	0	0		-	-	0	0	0
	30 ppm	0	0	0	1	0	0			0	0	0	0	0	0
	so ppm	U	U	U	U	U	U	0	0	1.	0	0	1	0	1
LIVATION	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	1	1	0	0	0	0	0	0	0	0	0	0	0	0

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CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

(HAN190)

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : FEMALE

PAGE : 80

Clinical sign	Group Name	Admir	istration	Week-day				 	 	 
		99-7	100-7	101-7	102-7	103-7	104-7	 	 	 
		1	1	1	1	1	1			
HEMORRHAGE	0 ppm	0	0	0	0	0	0			
	3 ppm	0	0	0	0	0	0			
	10 ppm	0	0	0	0	0	0			
	30 ppm	0	0	0	0	0	0			
IRREGULAR BREATHING	0 ppm	0	0	0	0	0	0			
	3 ppm	0	0	0	0	0	0			
	10 ppm	1	1	0	0	0	0			
	30 ppm	0	1	0	0	1	0			
BRADYPNEA	0 ppm	0	0	0	0	0	0			
	3 ppm	0	0	0	Ő	Ő	0			
	10 ppm	0	1	0	õ	Ő	0			
	30 ppm	0	0	0	0	0	Õ			
DEEP BREATHING	0 ppm	0	0	0	0	0	0			
	3 ppm	0	õ	0	0 0	0	0			
	10 ppm	0	0	0 0	õ	0	0			
	30 ppm	0	0	Ő	õ	0	0			
ABNORMAL RESPIRA. SOUND	0 ppm	0	0	0	0	0	0			
	3 ppm	Õ	0	0	0	0	0			
	10 ppm	õ	Ő	0	· 0	0	0			
	30 ppm	0	Ō	0	0	0	0			
SUBNORMAL TEMP	0 ppm	0	0	0	0	0	0			
	3 ppm	0	0	0	0	0 0	0			
	10 ppm	0	1	0	1	0				
	30 ppm	0	0	0	0	0	0			
ALIVATION	0 ppm	0	0	0	1		•			
	3 ppm	0	0	0 0	1	1	0			
	10 ppm	0	0	0	0	0	0			
	30 ppm	0	0	0	0	0 0	0			

(HAN190)

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, RAT : MALE

(2-YEAR STUDY)

BODY WEIGHT CHANGES (SUMMARY)

ALL ANIMALS

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PAGE: 1

ip Name	Administ	tratio	n week										
	0		1		2		3	4		5		6	- ·
0 ppm	122±	4	152±	6	180±	8	204± 10	221±	11	242±	12	256±	13
3 ppm	122±	4	152±	6	180±	8	202± 10	219±	11	$238\pm$	12	$252\pm$	14
10 ppm	122±	4	· 152±	6	180±	7	203± 9	$219\pm$	10	238±	11	$251\pm$	12
30 ppm	122±	4	152±	6	179±	7	201± 8	217±	9	$235\pm$	10	$249\pm$	12*
Significant differen	nce; *:P≦0.	05	** : P ≦ 0.0	01			Test of Dunnett						
N260)							·····						

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			A	LL ANIMALS	CHANGES	(SUMMARY)							
Admini	istration	week											
7		8		9		10		11		12		13	
270±	14	280±	15	289±	15	297±	16	304±	17	311±	16	317±	16
265±	14	276±	15	284±	16	292±	17	299±	17	$305\pm$	17	314±	19
264±	13*	274±	14	283±	15	291±	15	$298\pm$	16	305±	17	312±	17
261±	13**	271±	13**	279±	13**	$288\pm$	14*	295±	15*	300±	16**	307±	16*
	7 270 $\pm$ 265 $\pm$ 264 $\pm$ 261 $\pm$	Administration 7 270± 14 265± 14 264± 13* 261± 13**	Administration       week         7       8         270±       14       280±         265±       14       276±         264±       13*       274±         261±       13**       271±	Administration       week         7       8 $270 \pm$ 14 $280 \pm$ 15 $265 \pm$ 14 $276 \pm$ 15 $264 \pm$ 13* $274 \pm$ 14 $261 \pm$ 13** $271 \pm$ 13**	Administration       week       9         7       8       9         270 $\pm$ 14       280 $\pm$ 15       289 $\pm$ 265 $\pm$ 14       276 $\pm$ 15       284 $\pm$ 264 $\pm$ 13*       274 $\pm$ 14       283 $\pm$ 261 $\pm$ 13**       271 $\pm$ 13**       279 $\pm$	Administration       week       9 $7$ $8$ $9$ $270 \pm$ $14$ $280 \pm$ $15$ $289 \pm$ $15$ $265 \pm$ $14$ $276 \pm$ $15$ $284 \pm$ $16$ $264 \pm$ $13*$ $274 \pm$ $14$ $283 \pm$ $15$ $261 \pm$ $13**$ $271 \pm$ $13**$ $279 \pm$ $13**$	Administration       week       9       10 $7$ $8$ $9$ $10$ $270 \pm$ $14$ $280 \pm$ $15$ $289 \pm$ $15$ $297 \pm$ $265 \pm$ $14$ $276 \pm$ $15$ $284 \pm$ $16$ $292 \pm$ $264 \pm$ $13*$ $274 \pm$ $14$ $283 \pm$ $15$ $291 \pm$ $261 \pm$ $13**$ $271 \pm$ $13**$ $279 \pm$ $13**$ $288 \pm$	Administration       week       9       10 $7$ $8$ $9$ $10$ $270 \pm$ $14$ $280 \pm$ $15$ $289 \pm$ $15$ $297 \pm$ $16$ $265 \pm$ $14$ $276 \pm$ $15$ $284 \pm$ $16$ $292 \pm$ $17$ $264 \pm$ $13*$ $274 \pm$ $14$ $283 \pm$ $15$ $291 \pm$ $15$ $261 \pm$ $13**$ $271 \pm$ $13**$ $279 \pm$ $13**$ $288 \pm$ $14*$	Administration       week       9       10       11 $7$ $8$ $9$ $10$ $11$ $270 \pm$ $14$ $280 \pm$ $15$ $289 \pm$ $15$ $297 \pm$ $16$ $304 \pm$ $265 \pm$ $14$ $276 \pm$ $15$ $284 \pm$ $16$ $292 \pm$ $17$ $299 \pm$ $264 \pm$ $13*$ $274 \pm$ $14$ $283 \pm$ $15$ $291 \pm$ $15$ $298 \pm$ $261 \pm$ $13**$ $271 \pm$ $13**$ $279 \pm$ $13**$ $288 \pm$ $14*$ $295 \pm$	Administration       week       9       10       11 $7$ $8$ $9$ $10$ $11$ $270 \pm$ $14$ $280 \pm$ $15$ $289 \pm$ $15$ $297 \pm$ $16$ $304 \pm$ $17$ $265 \pm$ $14$ $276 \pm$ $15$ $284 \pm$ $16$ $292 \pm$ $17$ $299 \pm$ $17$ $264 \pm$ $13*$ $274 \pm$ $14$ $283 \pm$ $15$ $291 \pm$ $15$ $298 \pm$ $16$ $261 \pm$ $13**$ $271 \pm$ $13**$ $279 \pm$ $13**$ $288 \pm$ $14*$ $295 \pm$ $15*$	Administration       week       9       10       11       12 $7$ $8$ $9$ $10$ $11$ $12$ $270 \pm$ $14$ $280 \pm$ $15$ $289 \pm$ $15$ $297 \pm$ $16$ $304 \pm$ $17$ $311 \pm$ $265 \pm$ $14$ $276 \pm$ $15$ $284 \pm$ $16$ $292 \pm$ $17$ $299 \pm$ $17$ $305 \pm$ $264 \pm$ $13$ $274 \pm$ $14$ $283 \pm$ $15$ $291 \pm$ $15$ $298 \pm$ $16$ $305 \pm$ $261 \pm$ $13 * $ $271 \pm$ $13 * $ $279 \pm$ $13 * $ $288 \pm$ $14 *$ $295 \pm$ $15 *$ $300 \pm$	Administration       week       9       10       11       12 $7$ $8$ $9$ $10$ $11$ $12$ $270 \pm$ $14$ $280 \pm$ $15$ $297 \pm$ $16$ $304 \pm$ $17$ $311 \pm$ $16$ $265 \pm$ $14$ $276 \pm$ $15$ $284 \pm$ $16$ $292 \pm$ $17$ $299 \pm$ $17$ $305 \pm$ $17$ $264 \pm$ $13 *$ $274 \pm$ $14$ $283 \pm$ $15$ $291 \pm$ $15$ $298 \pm$ $16$ $305 \pm$ $17$ $261 \pm$ $13 * *$ $271 \pm$ $13 * *$ $279 \pm$ $13 * *$ $288 \pm$ $14 *$ $295 \pm$ $15 *$ $300 \pm$ $16 * *$	Administration       week       9       10       11       12       13 $270 \pm$ 14 $280 \pm$ 15 $289 \pm$ 15 $297 \pm$ 16 $304 \pm$ 17 $311 \pm$ 16 $317 \pm$ $265 \pm$ 14 $276 \pm$ 15 $289 \pm$ 16 $292 \pm$ 17 $299 \pm$ 17 $305 \pm$ 17 $314 \pm$ $264 \pm$ 13* $274 \pm$ 14 $283 \pm$ 15 $291 \pm$ 15 $298 \pm$ 16 $305 \pm$ 17 $312 \pm$ $261 \pm$ 13** $271 \pm$ $13**$ $279 \pm$ $13**$ $288 \pm$ $14*$ $295 \pm$ $15*$ $300 \pm$ $16**$ $307 \pm$

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PAGE : 2

BAIS 3

PAGE : 3

BAIS 3

p Name	Admin	istration	week											
	14		18		22		26		30		34		38	
0 ppm	324±	17	$340\pm$	19	354±	20	368±	20	378±	22	387±	23	$393\pm$	23
3 ppm	319±	19	337±	20	350±	22	365±	24	376±	25	$385\pm$	26	393±	26
10 ppm	317±	17	333±	18	347±	18	$359\pm$	19	$368\pm$	21	378±	21	384±	21
30 ppm	313±	16**	$328\pm$	17**	$341\pm$	18**	351±	19**	$360\pm$	19**	370±	20**	377±	20**
Significant differen	nce; *:P≦	0.05 *	* : P ≦ 0.0	01			Test of D	unnett						

(SUMMARY)

BODY WEIGHT CHANGES

ALL ANIMALS

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PAGE: 4

BAIS 3

Name	Administration	week					
	42	46	50	54	58	62	66
0 ppm	401± 24	406± 24	412± 24	416± 24	420± 25	422± 25	423± 27
3 ppm	400± 27	405± 27	411± 28	415± 28	417± 30	420± 29	419± 30
10 ppm	391± 22	395± 22	402± 22	407± 22	409± 23	411± 23	411± 25
30 ppm	385± 22**	390± 21**	397± 22**	401± 22**	404± 22**	402± 21**	401± 20**

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(SUMMARY)

(HAN260)

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BODY WEIGHT CHANGES

PAGE : 5

Name	Admin	istration '	week											
	70		74		78		82	······	86	· · · · · · · · · · · · · · · · · · ·	90		94	
0 ppm	427±	28	427±	32	426±	26	422±	23	421±	23	419±	25	413±	24
3 ppm	421±	31	419±	34	423±	29	421±	29	$423\pm$	30	$419\pm$	28	415±	35
10 ppm	414±	26	415±	30	$413\pm$	37	408±	26*	408±	26	406±	25*	403±	26
30 ppm	400±	19**	395±	22**	389±	28**	393±	34**	386±	31**	376±	27**	370±	39**
ignificant difference ;	* · D <		* : P ≤ 0.				Test of Du							

(SUMMARY)

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BODY WEIGHT CHANGES

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SEX : MALE PAGE : 6 Group Name Administration week\_ 98 102 104 0 ppm 412± 29 406± 42 401± 47 3 ppm 415± 35 413± 44 411± 50 10 ppm 395± 32  $395 \pm 37$ 392± 43 30 ррш 349± 57\*\* 347± 54\*\* 336± 33\*\*

(SUMMARY)

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

 (HAN260)
 BAIS 3

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BODY WEIGHT CHANGES

APPENDIX B 2

# BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

(2-YEAR STUDY)

PAGE : 7

Name	Admini	stration	week									
	0		1	2		3	4		5		6	
0 ppm	96±	3	110± 5	122±	5	133± 6	139±	7	150±	7	156±	8
3 ppm	96±	3	109± 4	122±	4	$132\pm 5$	$138\pm$	5	148±	7	154±	7
10 ppm	96±	3	110± 5	122±	5	132± 6	138±	6	148±	8	153±	9
30 ppm	96±	3	110± 4	121±	5	$132 \pm 5$	$137\pm$	5	147±	6	152±	7*
ignificant difference	; *:P≦(		** : P ≤ 0.01			Test of Dunnett						

### BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

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STUDY NO. : 0342 BODY WEIGHT CHANGES (SUMMARY) ANIMAL : RAT F344/DuCrj ALL ANIMALS UNIT : g REPORT TYPE : A1 104 SEX : FEMALE PAGE : 8 Group Name Administration week\_ 7 8 9 10 11 12 13 0 ppm  $162 \pm$ 9  $165 \pm 9$ 170± 9 176± 9 180± 10 182± 10 185± 11 3 ppm  $159 \pm$ 7 161± 7 166± 8 172± 8 175± 9 178± 9 182± 10 10 ppm  $158\pm$ 9\* 161± 10 166± 10\* 171± 10\*\* 174± 11\* 176± 11\*  $180 \pm 11$ 30 ppm  $157\pm$ 159± 8\*\* 7\*\*  $164 \pm$  $168 \pm$ 8\*\* 8\*\*  $171\pm$ 8\*\* 173± 8\*\* 177± 8\*\* Significant difference ;  $*: P \leq 0.05$ \*\* : P ≦ 0.01 Test of Dunnett (HAN260)

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BAIS 3

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PAGE : 9

p Name	Admini	stration	week											
			18		22		26		30		34		38	
0 ppm	188±	11	192±	11	197±	11	205±	13	211±	12	216±	15	217±	14
3 ррт	182±	9*	188±	11	195±	11	204±	12	209±	12	215±	13	216±	13
10 ppm	182±	11*	185±	12**	190±	12**	$198\pm$	13*	$203\pm$	14**	$208\pm$	16**	211±	16
30 mqq 08	179±	9 <b>*</b> *	183±	9 <b>*</b> *	188±	9 <b>*</b> *	195±	9**	200±	10**	$206\pm$	10**	206±	10**
Simificant diffore														
Significant differe	nce; *:P≦(	). 05 🔹	** : P ≦ 0.0	)1			Test of Du	innett						
260)														

(SUMMARY)

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BODY WEIGHT CHANGES

PAGE : 10

54 $232\pm$ 18 $234\pm$ 19 $228\pm$ 18	58 234 $\pm$ 19 235 $\pm$ 18	62 240± 20 239± 20	66 $243 \pm 22$ $244 \pm 21$
234± 19			
	235± 18	$239 \pm 20$	244± 21
228± 18			
	230± 19	$233 \pm 20$	$238\pm$ 21
$225 \pm 13$	226± 13*	229± 14*	$235 \pm 15$
	225± 13	225± 13 226± 13*	$225 \pm 13$ $226 \pm 13*$ $229 \pm 14*$

(SUMMARY)

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BODY WEIGHT CHANGES

ALL ANIMALS

(HAN260)

BAIS 3

PAGE : 11

ip Name	Admin	istration	week											
	70		74		78		82		86		90		94	
0 ppm	246±	23	$250\pm$	23	254±	23	$258\pm$	24	262±	25	266±	25	266±	26
3 ppm	250±	21	$254\pm$	20	$259\pm$	20	$262\pm$	22	266±	21	267±	24	$270\pm$	24
10 ppm	244±	22	247±	21	$252\pm$	22	$256\pm$	22	262±	22	$267\pm$	22	$267\pm$	22
30 ppm	239±	16	240±	18*	243±	21*	249±	21	$252\pm$	25	$256\pm$	24	$256\pm$	30
								·						
Significant difference	xe; *:P≦:	0.05	** : P ≦ 0.(	01			Test of Dun	nett						

BODY WEIGHT CHANGES (SUMMARY)

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ALL ANIMALS

BAIS 3

PORT TYPE : A1 104 K : FEMALE									PAGE : 1
oup Name	Admin	istration	week				 	 	
	98		102		104				
0 ppm	269±	25	$270\pm$	27	267±	27			
3 ppm	274±	19	272±	21	271±	22			
10 ppm	266±	22	267±	29	271±	26			
30 ppm	254±	20**	$255\pm$	20*	$251\pm$	24*			

## APPENDIX C 1

## FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(2-YEAR STUDY)

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

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PAGE : 1

p Name	Administration week									
	1	2	3	4	5	6	?			
0 mad	15.2± 0.9	15.8± 1.1	16.9± 1.1	17.5± 1.2	17.3± 1.3	17.1± 1.2	17.6± 1.3			
3 ppm	15.4± 1.0	$16.1 \pm 1.2$	17.0± 1.3	17.1± 1.2	16.8± 1.1	$16.5 \pm 1.3$	16.9± 1.0*			
10 ppm	15.3± 1.0	16.0± 1.1	16.9± 1.1	17.1± 1.1	16.8± 1.1	16.3± 1.1**	17.0± 1.2*			
30 ppm	15.1± 1.0	16.1± 1.1	17.5± 1.3*	$17.2 \pm 1.6$	17.1± 1.9	16.9± 1.4	17.1± 1.5			
Significant difference	e; *:P≦0.05	** : P ≦ 0.01		Test of Dunnett						

#### BAIS 3

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

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up Name	Administration	week					
	8	9	10	11	12	13	14
0 ppm	17.4± 1.3	17.1± 1.1	16.8± 1.0	16.8± 1.1	16.4± 0.9	16.6± 0.9	16.7± 0.8
3 ppm	16.8± 0.9	$16.6 \pm 1.0$	16.4± 1.0	16.2± 1.1*	15.7± 1.1**	16.2± 1.2	16.0± 1.2***
10 ppm	16.8± 1.1	16.6± 1.2	16.1± 1.0**	16.0± 1.2**	16.1± 1.2	16.2± 1.1	16.0± 1.1**
30 ppm	17.1± 1.4	16.6± 1.1	16.1± 1.0**	16.5± 1.4	16.2± 1.3	16.2± 1.2	15.9± 1.0**
Significant differe	ence ; * : $P \leq 0.05$	** : P ≦ 0.01		Test of Dunnett			

(HAN260)

BAIS 3

PAGE : 2

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

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PAGE : 3

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| oup Name            | Administration         | week          |           |                 |                |                |           |
|---------------------|------------------------|---------------|-----------|-----------------|----------------|----------------|-----------|
|                     | - 18                   | 22            | 26        | 30              | 34             | 38             | 42        |
| 0 ppm               | $16.4 \pm 1.1$         | 16.4± 0.9     | 16.8± 1.0 | 16.4± 1.0       | 16.9± 1.0      | 17.2± 1.1      | 17.4± 1.1 |
| 3 ppm               | 16.4± 1.0              | 16.2± 1.1     | 16.6± 1.2 | 16.3± 1.1       | 16.7± 1.0      | 17.2± 1.1      | 17.3± 1.1 |
| 10 ppm              | 16.2± 1.0              | 16.2± 0.9     | 16.7± 1.1 | 16.2± 1.1       | 16.7 $\pm$ 1.0 | $16.9 \pm 1.0$ | 17.0± 1.1 |
| 30 ppm              | 15.9± 1.1              | 16.1± 1.1     | 16.4± 1.1 | 16.3± 1.0       | 16.5± 0.9      | 16.7 $\pm$ 1.0 | 17.1± 1.0 |
|                     |                        |               |           |                 |                |                |           |
| Significant differe | ence; $*: P \leq 0.05$ | ** : P ≦ 0.01 |           | Test of Dunnett |                |                |           |
| Significant differe | ence; *: P ≦ 0.05      | ** : P ≦ 0.01 |           | Test of Dunnett |                |                |           |

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

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| Administration | week                                                             |                                                                                                                           |                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                         |  |
|----------------|------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
| 46             | 50                                                               | 54                                                                                                                        | 58                                                                                                                                                                                                                         | 62                                                                                                                                                                                                                                                                                                                                                    | 66                                                                                                                                                                                                                                                                                                                                                                                 | 70                                                                                                                                                                                                                                                                                                                                                                                                                      |  |
| 17.1± 1.1      | 17.4± 1.1                                                        | 17.4± 1.0                                                                                                                 | 17.5± 1.0                                                                                                                                                                                                                  | 17.8± 1.1                                                                                                                                                                                                                                                                                                                                             | 17.8± 1.9                                                                                                                                                                                                                                                                                                                                                                          | 17.9± 1.2                                                                                                                                                                                                                                                                                                                                                                                                               |  |
| 17.0± 0.9      | $17.2 \pm 1.0$                                                   | 17.4± 1.0                                                                                                                 | 17.3± 1.0                                                                                                                                                                                                                  | 17.6± 1.0                                                                                                                                                                                                                                                                                                                                             | 17.7± 1.0                                                                                                                                                                                                                                                                                                                                                                          | 17.8± 1.2                                                                                                                                                                                                                                                                                                                                                                                                               |  |
| $16.7 \pm 0.9$ | 16.9± 1.0*                                                       | 17.0± 0.9                                                                                                                 | 16.8± 1.0**                                                                                                                                                                                                                | 17.1± 1.1**                                                                                                                                                                                                                                                                                                                                           | 17.3± 0.9**                                                                                                                                                                                                                                                                                                                                                                        | 17.4± 1.2*                                                                                                                                                                                                                                                                                                                                                                                                              |  |
| 16.9± 0.9      | 16.9± 1.1*                                                       | 17.1± 1.0                                                                                                                 | 16.7± 1.0**                                                                                                                                                                                                                | 16.9± 0.9**                                                                                                                                                                                                                                                                                                                                           | 17.0± 1.8**                                                                                                                                                                                                                                                                                                                                                                        | 16.8± 1.1**                                                                                                                                                                                                                                                                                                                                                                                                             |  |
| e; *:P≦0.05    | *** : P ≤ 0.01                                                   |                                                                                                                           | Test of Dunnett                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                         |  |
|                | $46$ $17.1 \pm 1.1$ $17.0 \pm 0.9$ $16.7 \pm 0.9$ $16.9 \pm 0.9$ | $17.1 \pm 1.1$ $17.4 \pm 1.1$ $17.0 \pm 0.9$ $17.2 \pm 1.0$ $16.7 \pm 0.9$ $16.9 \pm 1.0*$ $16.9 \pm 0.9$ $16.9 \pm 1.1*$ | 46         50         54 $17.1\pm$ $1.1$ $17.4\pm$ $1.1$ $17.4\pm$ $1.0$ $17.0\pm$ $0.9$ $17.2\pm$ $1.0$ $17.4\pm$ $1.0$ $16.7\pm$ $0.9$ $16.9\pm$ $1.0*$ $17.0\pm$ $0.9$ $16.9\pm$ $0.9$ $16.9\pm$ $1.1*$ $17.1\pm$ $1.0$ | 46       50       54       58 $17.1 \pm 1.1$ $17.4 \pm 1.1$ $17.4 \pm 1.0$ $17.5 \pm 1.0$ $17.0 \pm 0.9$ $17.2 \pm 1.0$ $17.4 \pm 1.0$ $17.3 \pm 1.0$ $17.0 \pm 0.9$ $17.2 \pm 1.0$ $17.4 \pm 1.0$ $17.3 \pm 1.0$ $16.7 \pm 0.9$ $16.9 \pm 1.0 *$ $17.0 \pm 0.9$ $16.8 \pm 1.0 * *$ $16.9 \pm 0.9$ $16.9 \pm 1.1 *$ $17.1 \pm 1.0$ $16.7 \pm 1.0 * *$ | 46         50         54         58         62 $17.1 \pm 1.1$ $17.4 \pm 1.1$ $17.4 \pm 1.0$ $17.5 \pm 1.0$ $17.8 \pm 1.1$ $17.0 \pm 0.9$ $17.2 \pm 1.0$ $17.4 \pm 1.0$ $17.3 \pm 1.0$ $17.6 \pm 1.0$ $16.7 \pm 0.9$ $16.9 \pm 1.0^*$ $17.0 \pm 0.9$ $16.8 \pm 1.0^{**}$ $17.1 \pm 1.1^{**}$ $16.9 \pm 0.9$ $16.9 \pm 1.1^*$ $17.1 \pm 1.0$ $16.7 \pm 1.0^{**}$ $16.9 \pm 0.9^{**}$ | 46         50         54         58         62         66 $17.1\pm 1.1$ $17.4\pm 1.1$ $17.4\pm 1.0$ $17.5\pm 1.0$ $17.8\pm 1.1$ $17.8\pm 1.9$ $17.0\pm 0.9$ $17.2\pm 1.0$ $17.4\pm 1.0$ $17.3\pm 1.0$ $17.6\pm 1.0$ $17.7\pm 1.0$ $16.7\pm 0.9$ $16.9\pm 1.0*$ $17.0\pm 0.9$ $16.8\pm 1.0**$ $17.1\pm 1.1**$ $17.3\pm 0.9**$ $16.9\pm 0.9$ $16.9\pm 1.1*$ $17.1\pm 1.0$ $16.7\pm 1.0**$ $16.9\pm 0.9**$ $17.0\pm 1.8**$ |  |

PAGE : 4

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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PAGE : 5

| up Name              | Administration | week          |                                       |                 |            |           |            |
|----------------------|----------------|---------------|---------------------------------------|-----------------|------------|-----------|------------|
|                      | 74             | 78            | 82                                    | 86              | 90         | 94        | 98         |
| ngg O                | 17.8± 1.2      | 17.9± 1.6     | 17.9± 1.1                             | 17.3± 1.1       | 17.1± 1.3  | 16.1± 2.5 | 17.2± 1.3  |
| 3 ppm                | 17.4± 2.0      | 17.6± 1.1     | 17.9± 1.2                             | 17.4± 1.6       | 17.0± 1.3  | 16.9± 1.9 | 17.7± 1.6  |
| 10 ppm               | 17.2± 1.5*     | 17.2± 1.6*    | 16.7± 1.9**                           | 16.9± 1.0       | 16.4± 1.9* | 16.3± 0.9 | 16.5± 2.1  |
| 30 ppm               | 16.6± 1.5**    | 16.7± 1.9**   | 16.7± 1.5 <b>**</b>                   | 15.8± 1.5**     | 16.2± 1.7* | 16.1± 2.2 | 14.7± 5.4* |
|                      |                |               |                                       |                 |            |           |            |
| Significant differer | nce; *:P≦0.05  | ** : P ≦ 0.01 |                                       | Test of Dunnett |            |           |            |
| N260)                |                |               | · · · · · · · · · · · · · · · · · · · |                 |            |           |            |

BAIS 3

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS PAGE : 6

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|        | Administration |                |  |  |  |  |  |  |
|--------|----------------|----------------|--|--|--|--|--|--|
|        | 102            | 104            |  |  |  |  |  |  |
| 0 ppm  | 17.4± 1.5      | 17.2± 1.9      |  |  |  |  |  |  |
| 3 ppm  | 18.3± 1.6*     | 18.1± 1.6*     |  |  |  |  |  |  |
| 10 ppm | 17.0 $\pm$ 1.7 | 16.9± 1.2      |  |  |  |  |  |  |
| 30 ppm | 16.2± 1.7*     | 16.2 $\pm$ 2.1 |  |  |  |  |  |  |

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

 (HAN260)
 BAIS 3

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APPENDIX C 2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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| p Name | Administration | week           |           |                |           |             |             |
|--------|----------------|----------------|-----------|----------------|-----------|-------------|-------------|
|        | I              | 2              | 3         | 4              | 5         | 6           | 7           |
| 0 ppm  | 11.0± 0.8      | 10.8± 0.6      | 11.3± 0.9 | 11.7± 0.8      | 11.8± 0.9 | 11.5± 1.0   | 11.9± 1.0   |
| 3 ррт  | 11.3± 0.7      | 10.5± 0.7*     | 11.4± 0.8 | 11.4± 0.7      | 11.6± 0.9 | 11.2± 1.0   | 11.4± 1.1   |
| 10 ppm | 11.1± 0.8      | 10.7 $\pm$ 0.7 | 11.4± 0.9 | $11.5 \pm 1.2$ | 11.6± 1.9 | 11.0± 1.4** | 11.3± 1.0*  |
| 30 ppm | 11.0± 0.7      | 10.7± 0.7      | 11.6± 0.8 | 11.3± 0.7*     | 11.6± 0.8 | 11.2± 0.8   | 11.2± 1.0** |
|        |                |                |           |                |           |             |             |

(HAN260)

## FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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PAGE : 8

| Administration | week                                                 |                                                                                                                                 |                                                                                                                                                                   |                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                         |
|----------------|------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 8              | 9                                                    | 10                                                                                                                              | 11                                                                                                                                                                | 12                                                                                                                                                                                                                                                                       | 13                                                                                                                                                                                                                                                                                                                                                                                                                       | 14                                                                                                                                                                                                                                                                                                                                                                      |
| 10.9± 0.8      | 11.8± 1.0                                            | 12.1± 1.0                                                                                                                       | 12.2± 1.1                                                                                                                                                         | 11.5± 1.0                                                                                                                                                                                                                                                                | 11.6± 1.6                                                                                                                                                                                                                                                                                                                                                                                                                | 11.7± 1.8                                                                                                                                                                                                                                                                                                                                                               |
| 10.8± 0.9      | 11.4± 1.1                                            | 11.8± 0.9                                                                                                                       | 11.5± 0.9*                                                                                                                                                        | 11.1± 0.9                                                                                                                                                                                                                                                                | 11.6± 1.1                                                                                                                                                                                                                                                                                                                                                                                                                | 11.1± 0.9                                                                                                                                                                                                                                                                                                                                                               |
| 10.9± 0.9      | 11.1± 0.9**                                          | 11.1± 0.8**                                                                                                                     | 11.2± 1.0**                                                                                                                                                       | 11.3± 1.3                                                                                                                                                                                                                                                                | 11.4± 1.1                                                                                                                                                                                                                                                                                                                                                                                                                | 11.3± 1.2                                                                                                                                                                                                                                                                                                                                                               |
| 10.5± 0.7      | 11.0± 0.8**                                          | 10.9± 0.8**                                                                                                                     | 11.1± 0.8**                                                                                                                                                       | 11.1± 0.9                                                                                                                                                                                                                                                                | 11.2± 0.8                                                                                                                                                                                                                                                                                                                                                                                                                | 10.9± 0.9**                                                                                                                                                                                                                                                                                                                                                             |
|                |                                                      |                                                                                                                                 |                                                                                                                                                                   |                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                         |
|                | $\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$ | $10.9 \pm 0.8$ $11.8 \pm 1.0$ $10.8 \pm 0.9$ $11.4 \pm 1.1$ $10.9 \pm 0.9$ $11.1 \pm 0.9 * *$ $10.5 \pm 0.7$ $11.0 \pm 0.8 * *$ | 8       9       10 $10.9 \pm 0.8$ $11.8 \pm 1.0$ $12.1 \pm 1.0$ $10.8 \pm 0.9$ $11.4 \pm 1.1$ $11.8 \pm 0.9$ $10.9 \pm 0.9$ $11.1 \pm 0.9 * *$ $11.1 \pm 0.8 * *$ | 8       9       10       11 $10.9\pm 0.8$ $11.8\pm 1.0$ $12.1\pm 1.0$ $12.2\pm 1.1$ $10.8\pm 0.9$ $11.4\pm 1.1$ $11.8\pm 0.9$ $11.5\pm 0.9*$ $10.9\pm 0.9$ $11.1\pm 0.9**$ $11.1\pm 0.8**$ $11.2\pm 1.0**$ $10.5\pm 0.7$ $11.0\pm 0.8**$ $10.9\pm 0.8**$ $11.1\pm 0.8**$ | 8         9         10         11         12 $10.9\pm 0.8$ $11.8\pm 1.0$ $12.1\pm 1.0$ $12.2\pm 1.1$ $11.5\pm 1.0$ $10.8\pm 0.9$ $11.4\pm 1.1$ $11.8\pm 0.9$ $11.5\pm 0.9*$ $11.1\pm 0.9$ $10.9\pm 0.9$ $11.4\pm 1.1$ $11.8\pm 0.9$ $11.5\pm 0.9*$ $11.1\pm 0.9$ $10.9\pm 0.9$ $11.1\pm 0.9**$ $11.1\pm 0.8**$ $11.2\pm 1.0**$ $11.3\pm 1.3$ $10.5\pm 0.7$ $11.0\pm 0.8**$ $10.9\pm 0.8**$ $11.1\pm 0.8**$ $11.1\pm 0.9$ | 8910111213 $10.9\pm 0.8$ $11.8\pm 1.0$ $12.1\pm 1.0$ $12.2\pm 1.1$ $11.5\pm 1.0$ $11.6\pm 1.6$ $10.8\pm 0.9$ $11.4\pm 1.1$ $11.8\pm 0.9$ $11.5\pm 0.9*$ $11.1\pm 0.9$ $11.6\pm 1.1$ $10.9\pm 0.9$ $11.1\pm 0.9**$ $11.1\pm 0.8**$ $11.2\pm 1.0**$ $11.3\pm 1.3$ $11.4\pm 1.1$ $10.5\pm 0.7$ $11.0\pm 0.8**$ $10.9\pm 0.8**$ $11.1\pm 0.8**$ $11.1\pm 0.9$ $11.2\pm 0.8$ |

(HAN260)

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

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| up Name | Administration | week          |           |                 |           |            |           |
|---------|----------------|---------------|-----------|-----------------|-----------|------------|-----------|
|         | 18             | 22            | 26        | 30              | 34        | 38         | 42        |
| 0 ppm   | 11.2± 1.0      | 11.2± 1.0     | 11.6± 1.3 | 11.6± 1.1       | 11.7± 1.3 | 11.8± 1.0  | 11.8± 0.9 |
| 3 ppm   | 11.2± 1.1      | 11.2± 1.0     | 11.9± 1.9 | 11.6± 1.2       | 12.1± 1.4 | 11.9± 1.2  | 11.8± 1.0 |
| 10 ppm  | 10.6± 0.9*     | 10.8± 0.8*    | 11.5± 0.9 | 11.0± 1.0*      | 11.8± 1.3 | 11.6± 1.1  | 11.4± 0.8 |
| 30 ppm  | $10.9 \pm 0.9$ | 10.7± 0.9**   | 11.3± 1.2 | 11.2± 1.0       | 11.8± 1.1 | 11.2± 0.8* | 11.5± 1.0 |
|         |                |               |           |                 |           |            |           |
|         | ence; *:P≦0.05 | ** : P ≦ 0.01 |           | Test of Dunnett |           |            |           |
| 1260)   |                |               |           |                 |           |            |           |

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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| e6<br>3± 1.1 | 50<br>12.1± 1.0            | 54<br>11.9± 1.0 | 58<br>12.0± 0.9 | 62<br>12.6± 1.1 | 66<br>12.7± 1.1 | 70<br>13.0± 1.1 |
|--------------|----------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|              | 12.1± 1.0                  | 11.9± 1.0       | 12.0± 0.9       | 12.6± 1.1       | 12.7± 1.1       | $13.0 \pm 1.1$  |
|              |                            |                 |                 |                 |                 |                 |
| 1.1 ±        | 12.3± 1.6                  | 12.1± 1.3       | 11.9± 0.9       | 12.4± 1.0       | 12.8± 1.1       | 13.1± 1.0       |
| 3± 1.1       | 11.8± 1.1                  | 11.9± 1.1       | 11.6± 1.3       | 11.7土 1.0**     | 12.4± 1.0       | 12.8± 1.1       |
| 5± 0.8       | $12.0\pm 0.9$              | 11.7± 0.9       | 11.6± 0.7       | 11.5± 0.8**     | 12.4± 1.0       | 12.3± 1.2**     |
|              | $8 \pm 1.1$<br>$6 \pm 0.8$ |                 |                 |                 |                 |                 |

(HAN260)

BAIS 3

PAGE : 10

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

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PAGE : 11

| 74           |                                        |                                                                                                |                                                                                                                                             |                                                                                                                                                                                            |                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                         |
|--------------|----------------------------------------|------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|              | 78                                     | 82                                                                                             | 86                                                                                                                                          | 90                                                                                                                                                                                         | 94                                                                                                                                                                                                                                        | 98                                                                                                                                                                                                                                                                                      |
| 12.8± 1.2    | 12.8± 1.0                              | 12.9± 1.0                                                                                      | 12.9± 1.0                                                                                                                                   | 12.7± 1.0                                                                                                                                                                                  | 12.2± 1.0                                                                                                                                                                                                                                 | 13.0± 1.5                                                                                                                                                                                                                                                                               |
| 12.5± 0.9    | 12.8± 1.0                              | 12.9± 1.2                                                                                      | 12.4± 1.4                                                                                                                                   | 12.1± 1.3*                                                                                                                                                                                 | 12.1± 2.0                                                                                                                                                                                                                                 | 13.0± 1.3                                                                                                                                                                                                                                                                               |
| 12.2± 1.0*   | 12.5± 1.2                              | 12.5± 1.2                                                                                      | 12.7± 1.1                                                                                                                                   | 12.5± 1.0                                                                                                                                                                                  | $12.0 \pm 1.7$                                                                                                                                                                                                                            | 12.6± 1.4                                                                                                                                                                                                                                                                               |
| 11.8± 1.1**  | 12.0± 1.2**                            | 12.4± 1.0                                                                                      | 12.2± 1.0**                                                                                                                                 | 12.1± 1.3*                                                                                                                                                                                 | 11.7± 1.7*                                                                                                                                                                                                                                | 12.6± 1.9                                                                                                                                                                                                                                                                               |
| * : P < 0.05 | ** · P < 0.01                          |                                                                                                | Test of Duppett                                                                                                                             |                                                                                                                                                                                            |                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                         |
|              | 12.5± 0.9<br>12.2± 1.0*<br>11.8± 1.1** | $12.5 \pm 0.9$ $12.8 \pm 1.0$ $12.2 \pm 1.0*$ $12.5 \pm 1.2$ $11.8 \pm 1.1**$ $12.0 \pm 1.2**$ | $12.5 \pm 0.9$ $12.8 \pm 1.0$ $12.9 \pm 1.2$ $12.2 \pm 1.0*$ $12.5 \pm 1.2$ $12.5 \pm 1.2$ $11.8 \pm 1.1**$ $12.0 \pm 1.2**$ $12.4 \pm 1.0$ | $12.5 \pm 0.9$ $12.8 \pm 1.0$ $12.9 \pm 1.2$ $12.4 \pm 1.4$ $12.2 \pm 1.0*$ $12.5 \pm 1.2$ $12.5 \pm 1.2$ $12.7 \pm 1.1$ $11.8 \pm 1.1**$ $12.0 \pm 1.2**$ $12.4 \pm 1.0$ $12.2 \pm 1.0**$ | $12.5 \pm 0.9$ $12.8 \pm 1.0$ $12.9 \pm 1.2$ $12.4 \pm 1.4$ $12.1 \pm 1.3*$ $12.2 \pm 1.0*$ $12.5 \pm 1.2$ $12.5 \pm 1.2$ $12.7 \pm 1.1$ $12.5 \pm 1.0$ $11.8 \pm 1.1**$ $12.0 \pm 1.2**$ $12.4 \pm 1.0$ $12.2 \pm 1.0**$ $12.1 \pm 1.3*$ | $12.5 \pm 0.9$ $12.8 \pm 1.0$ $12.9 \pm 1.2$ $12.4 \pm 1.4$ $12.1 \pm 1.3*$ $12.1 \pm 2.0$ $12.2 \pm 1.0*$ $12.5 \pm 1.2$ $12.5 \pm 1.2$ $12.7 \pm 1.1$ $12.5 \pm 1.0$ $12.0 \pm 1.7$ $11.8 \pm 1.1**$ $12.0 \pm 1.2**$ $12.4 \pm 1.0$ $12.2 \pm 1.0**$ $12.1 \pm 1.3*$ $11.7 \pm 1.7*$ |

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS  $\sim$ 

| roup Name              | Administration        | week          |                 |                                       |
|------------------------|-----------------------|---------------|-----------------|---------------------------------------|
| ·····                  | 102                   | 104           |                 |                                       |
|                        |                       |               |                 |                                       |
| 0 ppm                  | $13.4 \pm 1.2$        | 12.9± 1.3     |                 | · · · · · · · · · · · · · · · · · · · |
| 3 ppm                  | $13.2 \pm 1.3$        | 12.7± 1.6     |                 |                                       |
| 10 ppm                 | 12.8± 2.2             | 13.1± 1.2     |                 |                                       |
|                        |                       | 13.1.4 1.2    |                 |                                       |
| 30 mad 10              | 12.3± 1.4**           | 11.9± 2.3     |                 |                                       |
|                        |                       |               |                 |                                       |
| Significant difference |                       |               |                 |                                       |
|                        | • <b>*</b> · Y ≥ 0.05 | ** : P ≦ 0.01 | Test of Dunnett |                                       |
| AN260)                 |                       |               |                 | DAT                                   |

BAIS 3

APPENDIX D 1

HEMATOLOGY : SUMMARY, RAT : MALE

| oup Name | NO. of<br>Animals | RED BL<br>1 O <sup>s</sup> / | 00D CELL<br>µl | HEMOGLO.<br>g⁄dl | BIN  | HEMATOC<br>% | RIT | MCV<br>f L |      | MCH<br>pg      |     | MCHC<br>g∕dℓ |     | PLATELE:<br>1 0 <sup>3</sup> /µJ |     |
|----------|-------------------|------------------------------|----------------|------------------|------|--------------|-----|------------|------|----------------|-----|--------------|-----|----------------------------------|-----|
| 0 ppm    | 39                | 8.38±                        | 1.39           | $13.9\pm$        | 2. 3 | 42.9±        | 6.1 | 51.6±      | 4.0  | 16 <b>.</b> 7± | 1.3 | 32.3±        | 1.1 | 868±                             | 209 |
| 3 ppm    | 40                | 7.93±                        | 1.32           | 13.0±            | 2.7  | 40.6±        | 7.0 | 51.3±      | 3. 2 | 16.2±          | 1.5 | 31.6±        | 1.9 | 1009±                            | 320 |
| 10 ppm   | 36                | $8.50\pm$                    | 1.49           | 13.8±            | 2.8  | 43.0±        | 7.5 | 50.8±      | 3.2  | 16.2±          | 1.3 | 32.0±        | 1.5 | 892±                             | 181 |
| 30 ppm   | 21                | 8.61±                        | 1.55           | 13.9±            | 3.1  | 43.5±        | 8.4 | 50.4±      | 2.8  | 16.0±          | 1.5 | 31.8±        | 1.8 | $852\pm$                         | 215 |

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(HCL070)

| roup Name | NO. of<br>Animals | ₩BC<br>1 0³∕µℓ  | Dif<br>N-BAND | ferentia | 1 WBC (9<br>N-SEG | 6) | EOSINO |    | BASO |   | MONO       |   | LYMPHO |    | PAGE |   |
|-----------|-------------------|-----------------|---------------|----------|-------------------|----|--------|----|------|---|------------|---|--------|----|------|---|
| mqq O     | 39                | 6.19± 2.46      | 1±            | 1        | 42±               | 11 | 2±     | 2  | 0±   | 0 | 5±         | 3 | 47±    | 10 | 3±   | 5 |
| 3 ppm     | 40                | 5.84± 1.77      | 1±            | 1        | 41±               | 11 | 2±     | 2  | 0±   | 0 | 5±         | 2 | 47±    | 10 | 4±   | 5 |
| 10 ppm    | 36                | $5.52 \pm 1.37$ | 1土            | 1        | 40±               | 9  | 2±     | 1  | 0±   | 0 | 4±         | 2 | 48±    | 10 | 4土   | 5 |
| 30 ppm    | 21                | 7.47± 2.89      | 1±            | 2        | 45±               | 14 | 1±     | 1* | 0±   | 0 | <b>4</b> ± | 2 | 42±    | 14 | 6±   | 8 |

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APPENDIX D 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

| oup Name | NO. of<br>Animals | RED BL<br>1 O <sup>S</sup> / | 00D CELL<br>µl | HEMOGLO<br>g⁄dl | BIN    | HEMATOO<br>% | CRIT  | MCV<br>f L |      | MCH<br>Pg |      | MCHC<br>g∕dl |      | PLATELE<br>1 0 <sup>3</sup> ⁄µ |     |
|----------|-------------------|------------------------------|----------------|-----------------|--------|--------------|-------|------------|------|-----------|------|--------------|------|--------------------------------|-----|
| 0 ppm    | 41                | 8.25±                        | 0.99           | 15.0±           | 1.6    | 44.6±        | 4. 1  | 54.7±      | 5.2  | 18.3±     | 1.3  | 33.6±        | 0.8  | $605\pm$                       | 84  |
| 3 ppm    | 38                | 8.27±                        | 0.50           | 14.9±           | 1.0    | 44.7±        | 2.5   | 54.1±      | 1.9  | 18.1±     | 0. 7 | 33.4±        | 0.7  | 603±                           | 109 |
| 10 ppm   | 39                | 8.18±                        | 0.66           | 14.8±           | 1.2    | 44. 2±       | 3.0   | 54. 2±     | 2. 3 | 18.1±     | 0.7  | 33.4±        | 0.6  | 618±                           | 69  |
| 30 ppm   | 32                | 7.67±                        | 1.21**         | 14.0±           | 2. 0** | 42.3±        | 5.0** | 55.9±      | 6.0  | 18.4±     | 1. 3 | 33.0±        | 1.6* | 656±                           | 135 |

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STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj MEASURE. TIME : 1

# HEMATOLOGY (SUMMARY)

ALL ANIMALS (105W)

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SEX : FEMALE REPORT TYPE : A1 \_\_\_\_

PAGE: 4

| roup Name | NO. of<br>Animals | ₩BC<br>1 0³∕µl | Dif<br>N-BAND | fferentia | I WBC (%<br>N-SEG | 5) | EOSINO |   | BASO |   | MONO |   | LYMPHO  |    | OTHER |    |
|-----------|-------------------|----------------|---------------|-----------|-------------------|----|--------|---|------|---|------|---|---------|----|-------|----|
| 0 ppm     | 41                | 4.50± 11.04    | 1±            | 1         | 39±               | 12 | 2±     | 1 | 0±   | 0 | 5±   | 2 | 48±     | 11 | 5±    | 16 |
| 3 ppm     | 38                | 3.02± 2.41     | 1±            | 1         | 39±               | 13 | 2±     | 1 | 0±   | 0 | 5±   | 2 | 50±     | 13 | 3±    | 5  |
| 10 ppm    | 39                | 3.54± 3.21     | 1±            | 1         | 37±               | 11 | 2±     | 1 | 0±   | 0 | 5±   | 2 | $53\pm$ | 10 | 3±    | 4  |
| 30 ppm    | 32                | 8.00± 15.25**  | 1±            | 2         | $38\pm$           | 16 | 1±     | 1 | 0±   | 0 | 4±   | 2 | 45±     | 17 | 10±   | 23 |

(HCL070)

# APPENDIX E 1

# BIOCHEMISTRY : SUMMARY, RAT : MALE

| ıp Name | NO. of<br>Animals | TOTAL F<br>g∕dl | PROTEIN | ALBUMIN<br>g⁄dl |      | A/G RAT | 10    | T-BILII<br>mg∕dl |       | GLUCOSE<br>mg⁄dl | •  | T−CHOLE<br>mg∕dℓ | STEROL | TRIGLYC<br>mg∕dl | ERIDE |
|---------|-------------------|-----------------|---------|-----------------|------|---------|-------|------------------|-------|------------------|----|------------------|--------|------------------|-------|
| 0 ppm   | 39                | 6.3±            | 0.6     | 3.3±            | 0.3  | 1.1±    | 0.1   | 0.21±            | 0. 22 | $146\pm$         | 29 | $187\pm$         | 62     | 118±             | 85    |
| 3 ppm   | 41                | 6.4±            | 0.5     | 3.4±            | 0.3  | 1.1±    | 0.1   | 0.16±            | 0.06  | 155±             | 23 | 193±             | 68     | $133\pm$         | 77    |
| 10 ppm  | 37                | 6.4±            | 0.3     | 3.4±            | 0, 3 | 1.1±    | 0.1   | 0.18±            | 0.03  | $157\pm$         | 22 | 189±             | 73     | 129±             | 87    |
| 30 ppm  | 21                | 6.3±            | 0.8     | 3.1±            | 0.3* | 1.0±    | 0.2** | 0.18±            | 0.08  | $135\pm$         | 35 | 209±             | 71     | $167\pm$         | 177   |

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| up Name | NO. of<br>Animals | PHOSPHO<br>mg∕dl | LIPID | GOT<br>IU/J | 2   | GPT<br>IU/L |    | LDH<br>IU/1 |    | ALP<br>IU/J | 2   | G-GTP<br>IU/L |    | CPK<br>IU/l |    |
|---------|-------------------|------------------|-------|-------------|-----|-------------|----|-------------|----|-------------|-----|---------------|----|-------------|----|
| 0 ppm   | 39                | 269±             | 93    | 114±        | 125 | 48±         | 36 | 215±        | 97 | 208±        | 98  | 11±           | 7  | 105±        | 36 |
| 3 ppm   | 41                | 280±             | 82    | 75±         | 41  | $34\pm$     | 14 | 193±        | 54 | 207±        | 72  | 11土           | 6  | 93±         | 17 |
| 10 ppm  | 37                | 274±             | 104   | 78±         | 28  | 36±         | 15 | 195±        | 46 | 200±        | 61  | 13±           | 8  | 91±         | 12 |
| 30 ppm  | 21                | $332\pm$         | 167   | 110±        | 81  | 50±         | 33 | $218\pm$    | 73 | 232±        | 128 | 14±           | 10 | 106±        | 23 |

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(HCL074)

| oup Name | NO. of<br>Animals | UREA NI<br>mg∕d£ | TROGEN | CREATIN<br>mg∕dl | INE | SODIUM<br>mEq∕£ | ····· | POTASSI<br>mEq / J |      | CHLORIDE<br>mEq⁄l |     | CALCIUN<br>mg⁄dl | 1   | INORGAN<br>mg⁄dl | IC PHOSPHORU |
|----------|-------------------|------------------|--------|------------------|-----|-----------------|-------|--------------------|------|-------------------|-----|------------------|-----|------------------|--------------|
| 0 ppm    | 39                | 21.1±            | 5.1    | 0.6±             | 0.1 | 143±            | 2     | 3.9±               | 0.3  | 106±              | 2   | 10.2±            | 0.4 | 4.2±             | 0.7          |
| 3 ppm    | 41                | 22.1±            | 5.8    | 0.5±             | 0.1 | $143\pm$        | 2     | 3.9±               | 0.4  | 106±              | 2   | 10.3±            | 0.3 | 4.4±             | 0.6          |
| 10 ppm   | 37                | 21.3±            | 5.0    | 0.5±             | 0.1 | 143±            | 1     | 3.8±               | 0, 3 | 106±              | 2   | 10.3±            | 0.4 | 4.2±             | 0.6          |
| 30 ppm   | 21                | 22.8±            | 4.4    | 0.5±             | 0.1 | 142±            | 1     | 3.9±               | 0.5  | 104±              | 2** | 10.3±            | 0.5 | 4.5±             | 0.8          |

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APPENDIX E 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

| Name   | NO. of<br>Animals | TOTAL F<br>g∕dl |     | ALBUMIN<br>g∕dl |      | A/G RAT | 010 | T-BILI<br>mg∕d£ |      | GLUCOSE<br>mg⁄dl |    | T-CHOLE<br>mg∕dl | STEROL | TRIGLYC<br>mg∕dℓ | ERIDE |
|--------|-------------------|-----------------|-----|-----------------|------|---------|-----|-----------------|------|------------------|----|------------------|--------|------------------|-------|
| 0 ppm  | 41                | 6.8±            | 0.4 | 4.0±            | 0.3  | 1.5±    | 0.2 | 0.16±           | 0.09 | 144±             | 15 | 140±             | 27     | 75±              | 57    |
| 3 ppm  | 38                | 6.8±            | 0.4 | 3.9±            | 0.4  | 1.4±    | 0.2 | 0.15±           | 0.05 | $143\pm$         | 18 | 158±             | 65     | $105\pm$         | 161   |
| 10 ppm | 39                | 6.7±            | 0.3 | 4.0±            | 0, 3 | 1.4±    | 0.2 | 0.15±           | 0.03 | $147\pm$         | 13 | $140\pm$         | 29     | 74土              | 32    |
| 30 ppm | 32                | 6.6±            | 0.4 | 3.8±            | 0.2  | 1.4±    | 0.2 | 0.16±           | 0.06 | $143\pm$         | 23 | $149\pm$         | 67     | 87±              | 72    |

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| Name   | NO. of<br>Animals | PHOSPHC<br>mg/dl | DLIPID | GOT<br>IU/J | ٤   | GPT<br>IU/1 | ]  | LDH<br>IU/. | ٤   | ALP<br>IU/ <b>L</b> |    | G-GTP<br>IU∕ℓ |   | CPK<br>IU/L |    |
|--------|-------------------|------------------|--------|-------------|-----|-------------|----|-------------|-----|---------------------|----|---------------|---|-------------|----|
| 0 ppm  | 41                | 253±             | 41     | 138±        | 152 | 57±         | 27 | 264±        | 206 | 132±                | 57 | $5\pm$        | 4 | 96±         | 36 |
| 3 ppm  | 38                | $275\pm$         | 103    | 139±        | 66  | 61±         | 26 | 265±        | 93  | 136±                | 66 | 5±            | 2 | 95±         | 27 |
| 10 ppm | 39                | $251\pm$         | 49     | $151\pm$    | 79  | 63±         | 31 | 287±        | 154 | 124±                | 51 | $5\pm$        | 3 | 93±         | 40 |
| 30 ppm | 32                | $262\pm$         | 96     | $157\pm$    | 114 | $55\pm$     | 23 | 307±        | 245 | $151\pm$            | 72 | 6±            | 5 | 100±        | 50 |

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STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj MEASURE. TIME : 1

## BIOCHEMISTRY (SUMMARY)

ALL ANIMALS (105W)

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| cup Name | NO. of<br>Animals | UREA NI<br>mg⁄dl | TROGEN | CREATIN<br>mg⁄dl | INE  | SODIUM<br>mEq⁄l |   | POTASSI<br>mEq⁄. |     | CHLORIDE<br>mEq⁄2 |   | CALCIUN<br>mg⁄dl | [   | INORGAN<br>mg∕dl | NIC PHOSPHORUS |
|----------|-------------------|------------------|--------|------------------|------|-----------------|---|------------------|-----|-------------------|---|------------------|-----|------------------|----------------|
| 0 ppm    | 41                | .18.8±           | 2. 1   | 0.5±             | 0.1  | 142±            | 1 | 3.6±             | 0.4 | 104±              | 2 | 10.2±            | 0.3 | 3.8±             | 0.7            |
| 3 ppm    | 38                | 19.3±            | 2.5    | 0.5±             | 0.1  | 141±            | 2 | 3.6±             | 0.4 | 104±              | 2 | 10.4±            | 0.5 | 4.1±             | 0.7            |
| 10 ppm   | 39                | 18.2±            | 1.6    | 0.5±             | 0.1  | 141±            | 1 | 3.4±             | 0.4 | 104±              | 2 | 10.2±            | 0.3 | 3.9±             | 0.7            |
| 30 ppm   | 32                | 18.0±            | 2.4    | 0.5±             | 0. 1 | 142±            | 1 | 3.5±             | 0.4 | 104±              | 2 | 10.1±            | 0.4 | 4.1±             | 0.5            |

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APPENDIX F 1

URINALYSIS : SUMMARY, RAT : MALE

| oup Name | NO. of  | Hq   |     |     |     |     |     |     |     | Prote      | əin |            |     | Glue | ose |       |        | Ketc | one bo | dv  |        | Bi | lirubin |       |  |
|----------|---------|------|-----|-----|-----|-----|-----|-----|-----|------------|-----|------------|-----|------|-----|-------|--------|------|--------|-----|--------|----|---------|-------|--|
| ····.    | Animals | 5, 0 | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 | CHI | - <u>+</u> | : + | · 2+ 3+ 4+ | CHI |      | ± + | 2+ 3+ | 4+ CHI |      | ± +    |     | 4+ CHI |    | + 2+ 3  | + CHI |  |
| 0 ppm    | 40      | 0    | 1   | 2   | 5   | 26  | 6   | 0   |     | 0 (        | ) ( | 0 1 13 26  |     | 40   | 0 0 | 0 0   | 0      | 36   | 31     | 0 0 | 0      | 39 | 1 0     | 0     |  |
| 3 ppm    | 42      | 0    | 2   | 4   | 8   | 25  | 3   | 0   |     | 0 0        | ) ( | 0 4 10 28  |     | 42   | 0 0 | 0 0   | 0      | 40   | 1 1    | 0 0 | 0      | 40 | 2 0     | 0     |  |
| 10 ppm   | 38      | 0    | 0   | 2   | 4   | 21  | 9   | 2   |     | 0 0        | ) ( | 0 1 12 25  |     | 38   | 0 0 | 0 0   | 0      | 38   | 0 0    | 0 0 | 0      | 38 | 0 0     | 0     |  |
| 30 ppm   | 23      | 0    | 1   | 5   | 2   | 9   | 6   | 0.  |     | 0 0        | ) ( | 0 3 20     |     | 23   | 0 0 | 0 0   | 0      | 20   | 2 1    | 0 0 | 0      | 22 | 1 0     | 0     |  |

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| oup Name | NO. of<br>Animals | Occult blood<br>$-\pm +2+3+$ CHI | Urobilinogen<br>± + 2+ 3+ 4+ CHI |   |  |
|----------|-------------------|----------------------------------|----------------------------------|---|--|
| 0 ppm    | 40                | 40 0 0 0 0                       | 40 0 0 0 0                       | - |  |
| 3 ppm    | 42                | 40 0 1 0 1                       | 42 0 0 0 0                       |   |  |
| 10 ppm   | 38                | 38 0 0 0 0                       | 38 0 0 0 0                       |   |  |
| 30 ppm   | 23                | 19 1 0 0 3 *                     | 23 0 0 0 0                       |   |  |

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APPENDIX F 2

URINALYSIS : SUMMARY, RAT : FEMALE

| roup Name | NO - 6            | 11         |     |     | ····· |     |     |         | D                                 |                               |                                   |                            |
|-----------|-------------------|------------|-----|-----|-------|-----|-----|---------|-----------------------------------|-------------------------------|-----------------------------------|----------------------------|
| roup wame | NO. of<br>Animals | рН<br>5. 0 | 6.0 | 6.5 | 7.0   | 7.5 | 8.0 | 3.5 CHI | Protein<br>- $\pm$ + 2+ 3+ 4+ CHI | Glucose<br>- ± + 2+ 3+ 4+ CHI | Ketone body<br>- ± + 2+ 3+ 4+ CHI | Bilirubin<br>— + 2+ 3+ CHI |
| 0 ppm     | 41                | 0          | 0   | 1   | 7     | 10  | 17  | 6       | 1 3 7 10 14 6                     | 41 0 0 0 0 0                  | 35 4 1 1 0 0                      | 40 1 0 0                   |
| 3 ppm     | 38                | 0          | 0   | 3   | 4     | 12  | 18  | 1       | 0 1 7 12 8 10                     | 38 0 0 0 0 0                  | 31 5 2 0 0 0                      | 38 0 0 0                   |
| 10 ppm    | 39                | 0          | 0   | 0   | 6     | 12  | 21  | 0       | 0 3 2 8 19 7                      | 39 0 0 0 0 0                  | 24 15 0 0 0 0 *                   | 39 0 0 0                   |
| 30 ppm    | 32                | 0          | 1   | 2   | 3     | 11  | 10  | 5       | 0 0 2 7 16 7                      | 32 0 0 0 0 0                  | 18 13 1 0 0 0 *                   | 31 1 0 0                   |

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(HCL101)

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| STUDY NO. : 034<br>ANIMAL : RAT<br>MEASURE. TIME<br>SEX : FEMALE | ⊺ F344/DuCrj<br>∶ 1 | Type : A1                                 | URINALYSIS                       |                    | PAGE: 4 |
|------------------------------------------------------------------|---------------------|-------------------------------------------|----------------------------------|--------------------|---------|
| Group Name                                                       | NO. of<br>Animals   | Occult blood<br>$- \pm + 2 \pm 3 \pm$ CHI | Urobilinogen<br>± + 2+ 3+ 4+ CHI |                    |         |
| 0 ppm                                                            | 41                  | 41 0 0 0 0                                | 41 0 0 0 0                       |                    |         |
| 3 ppm                                                            | 38                  | 36 0 0 2 0                                | 38 0 0 0 0                       |                    |         |
| 10 ppm                                                           | 39                  | 36 2 0 1 0                                | 39 0 0 0 0                       |                    |         |
| 30 ppm                                                           | 32                  | 29 1 0 0 2                                | 32 0 0 0 0                       |                    |         |
| Significan                                                       | t difference        | ; * : P ≦ 0.05 **                         | : P ≤ 0.01                       | Test of CHI SQUARE |         |
| (HCL101)                                                         |                     |                                           |                                  |                    | BAIS 3  |

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APPENDIX G 1

GROSS FINDINGS : SUMMARY, RAT : MALE

ALL ANIMALS

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

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PAGE: 1

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| )rgan      | Findings    | Group Name<br>NO. of Animals | 0 p<br>50 (%) | pm<br>50 | 3 ppm<br>(%) | 50 | 10 ppm<br>(%) | 50 | 30 ppm<br>(%) |
|------------|-------------|------------------------------|---------------|----------|--------------|----|---------------|----|---------------|
| skin/app   | nodule      |                              | 3 (6)         | ) 4      | (8)          | 5  | ( 10)         | 12 | (24)          |
|            | scab        |                              | 0 ( 0)        | ) 1      | (2)          | 0  | ( 0)          | 0  | ( 0)          |
| subcutis   | edema       |                              | 0 ( 0)        | ) 0      | ( 0)         | 1  | (2)           | 0  | ( 0)          |
|            | jaundice    |                              | 0 ( 0)        | ) 0      | ( 0)         | 0  | ( 0)          | 1  | (2)           |
|            | nodule      |                              | 1 ( 2         | ) 0      | ( 0)         | 0  | ( 0)          | 0  | ( 0)          |
|            | mass        |                              | 10 ( 20)      | ) 8      | (16)         | 11 | (22)          | 14 | (28)          |
| ung        | red .       |                              | 1 (2          | ) 0      | ( 0)         | 0  | ( 0)          | 1  | (2)           |
|            | white zone  |                              | 0 ( 0         | ) 1      | (2)          | 4  | (8)           | 2  | ( 4)          |
|            | red zone    |                              | 0 ( 0         | ) 0      | ( 0)         | 0  | ( 0)          | 1  | (2)           |
|            | yellow zone |                              | 0 ( 0         | ) 1      | (2)          | 0  | ( 0)          | 0  | ( 0)          |
|            | red patch   |                              | 0 ( 0         | ) 1      | (2)          | 0  | ( 0)          | 1  | (2)           |
|            | nodule      |                              | 5 (10         | ) 2      | ( 4)         | 0  | ( 0)          | 0  | ( 0)          |
|            | voluminus   |                              | 0 ( 0         | ) 0      | ( 0)         | 0  | ( 0)          | 1  | (2)           |
| lymph node | enlarged    |                              | 2 (4          | ) 0      | ( 0)         | 0  | ( 0)          | 1  | (2)           |
| spleen     | enlarged    |                              | 9 (18         | ) 3      | (6)          | 3  | (6)           | 4  | (8)           |
|            | white zone  |                              | 0 ( 0         | ) 0      | ( 0)         | 1  | (2)           | 1  | (2)           |
|            | nodule      |                              | 0 ( 0         | ) 0      | ( 0)         | 0  | ( 0)          | 1  | (2)           |
|            | deformed    |                              | 0 ( 0         | ) 1      | (2)          | 0  | ( 0)          | 0  | ( 0)          |
| leart      | white zone  |                              | 0 ( 0         | ) 0      | ( 0)         | 1  | (2)           | 0  | ( 0)          |
|            | fluid:red   |                              | 0 ( 0         | ) 0      | ( 0)         | 0  | ( 0)          | 1  | (2)           |
|            | fluid:brown |                              | 0 ( 0         | ) 0      | ( 0)         | 0  | ( 0)          | 1  | (2)           |
| alivary gl | nodule      |                              | 0 ( 0         | ) 0      | (0)          | 2  | (4)           | 0  | (0)           |

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

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| rgan       | Findings               | Group Name<br>NO. of Animals 50 | 0 ppm<br>0 (%) | 3 ppm<br>50 (%) | 10 ppm<br>50 (%) | 30 ppm<br>50 (%) |
|------------|------------------------|---------------------------------|----------------|-----------------|------------------|------------------|
| prestomach | nodule                 | 1                               | 0 ( 0)         | 0 ( 0)          | 1 (2)            | 0 ( 0)           |
|            | ulcer                  |                                 | 1 (2)          | 0 ( 0)          | 0 ( 0)           | 1 (2)            |
| l stomach  | black zone             | (                               | 0 ( 0)         | 0 ( 0)          | 0 ( 0)           | 1 (2)            |
|            | ulcer                  | ſ                               | 0 ( 0)         | 0 ( 0)          | 0 ( 0)           | 1 (2)            |
|            | erosion                |                                 | 1 (2)          | 0 ( 0)          | 0 ( 0)           | 0 ( 0)           |
| omach      | nodule                 | (                               | 0 ( 0)         | 1 ( 2)          | 0 ( 0)           | 0 ( 0)           |
| all intes  | red zone               |                                 | 0 ( 0)         | 0 ( 0)          | 0 ( 0)           | 1 (2)            |
|            | nodule                 |                                 | 0 ( 0)         | 0 ( 0)          | 0 ( 0)           | 1 ( 2)           |
| ver        | enlarged               |                                 | 0 ( 0)         | 0 ( 0)          | 1 (2)            | 0 ( 0)           |
|            | pale                   |                                 | 1 (2)          | 0 ( 0)          | 0 ( 0)           | 0 ( 0)           |
|            | nodule                 |                                 | 1 (2)          | 3 ( 6)          | 1 (2)            | 0 ( 0)           |
|            | rough                  |                                 | 5 (10)         | 1 (2)           | 2 (4)            | 3 (6)            |
|            | herniation             |                                 | 5 (10)         | 9 (18)          | 6 (12)           | 3 (6)            |
| ncreas     | nodule                 |                                 | 2 (4)          | 0 ( 0)          | 0 ( 0)           | 0 ( 0)           |
| idney      | enlarged               |                                 | 0 ( 0)         | 0 ( 0)          | 0 ( 0)           | 1 (2)            |
|            | cyst                   |                                 | 0 ( 0)         | 0 ( 0)          | 0 ( 0)           | 1 (2)            |
|            | granular               | 1                               | 8 (36)         | 19 ( 38)        | 20 (40)          | 16 (32)          |
| in bladd   | nodule                 |                                 | 0 ( 0)         | 0 ( 0)          | 0 ( 0)           | 1 (2)            |
|            | urine:marked retention |                                 | 1 (2)          | 0 ( 0)          | 0 ( 0)           | 1 ( 2)           |
| tuitary    | enlarged               |                                 | 2 (4)          | 4 ( 8)          | 1 (2)            | 4 (8)            |
|            | red zone               |                                 | 3 (6)          | 3 (6)           | 3 ( 6)           | 1 (2)            |
|            | nodule                 |                                 | 4 (8)          | 5 (10)          | 3 (6)            | 7 (14)           |

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

PAGE : 3

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| rgan       | Findings      | Group Name 0 ppm<br>NO. of Animals 50 (%) | 3 ppm<br>50 (%) | 10 ppm<br>50 (%) | 30 ppm<br>50 (%) |
|------------|---------------|-------------------------------------------|-----------------|------------------|------------------|
| hyroid     | enlarged      | 3 ( 6)                                    | 2 ( 4)          | 2 ( 4)           | 6 (12)           |
| drenal     | enlarged      | 1 (2)                                     | 1 ( 2)          | 2 ( 4)           | 1 (2)            |
| estis      | atrophic      | 0 ( 0)                                    | 0 ( 0)          | 3 (6)            | 1 (2)            |
|            | nodule        | 38 (76)                                   | 39 (78)         | 41 (82)          | 44 (88)          |
| rain       | red zone      | 0 ( 0)                                    | 0 ( 0)          | 1 ( 2)           | 1 ( 2)           |
|            | hemorrhage    | 0 ( 0)                                    | 1 ( 2)          | 0 ( 0)           | 0 ( 0)           |
|            | deformed      | 0 ( 0)                                    | 0 ( 0)          | 0 ( 0)           | 1 (2)            |
| pinal cord | hemorrhage    | 0 ( 0)                                    | 1 (2)           | 0 ( 0)           | 0 ( 0)           |
| уe         | turbid        | 0 ( 0)                                    | 0 ( 0)          | 0 ( 0)           | 2 ( 4)           |
|            | white         | 3 ( 6)                                    | 0 ( 0)          | 1 ( 2)           | 2 ( 4)           |
|            | red           | 0 ( 0)                                    | 0 ( 0)          | 0 ( 0)           | 1 ( 2)           |
|            | nodule        | 0 ( 0)                                    | 0 ( 0)          | 0 ( 0)           | 1 (2)            |
| ymbal gl   | nodule        | 0 ( 0)                                    | 3 (6)           | 1 (2)            | 2 ( 4)           |
| nuscle     | nodule        | 0 ( 0)                                    | 0 ( 0)          | 1 ( 2)           | 0 ( 0)           |
| one        | nodule        | 0 ( 0)                                    | 1 (2)           | 0 ( 0)           | 0 ( 0)           |
| eritoneum  | nodule        | 2 ( 4)                                    | 5 (10)          | 9 (18)           | 18 ( 36)         |
|            | thick         | 0 ( 0)                                    | 0 ( 0)          | 0 ( 0)           | 1 ( 2)           |
| etroperit  | mass          | 0 ( 0)                                    | 0 ( 0)          | 1 ( 2)           | 1 ( 2)           |
|            | cyst          | 0 ( 0)                                    | 0 ( 0)          | 1 (2)            | 0 ( 0)           |
| bdominal c | hemorrhage    | 0 ( 0)                                    | 0 ( 0)          | 1 ( 2)           | 0 ( 0)           |
|            | pleural fluid | 0 ( 0)                                    | 0 ( 0)          | 0 ( 0)           | 1 ( 2)           |
|            | ascites       | 1 ( 2)                                    | 1 (2)           | 5 (10)           | 11 (22)          |

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

| Organ       | Findings        | Group Name<br>NO. of Animals 50 | 0 ppm<br>(%) | 3 pj<br>50 (%) |      | 10 ppm<br>(%) | 50 | 30 ppm<br>(%) |
|-------------|-----------------|---------------------------------|--------------|----------------|------|---------------|----|---------------|
| nesenterium | mass            | 1                               | (2)          | 0 ( 0)         | ) 0  | ( 0)          | 0  | ( 0)          |
| thoracic ca | hemorrhage      | 0                               | ( 0)         | 0 ( 0)         | ) 1  | (2)           | 0  | ( 0)          |
|             | nodule          | 0                               | ( 0)         | 0 ( 0)         | ) 1  | (2)           | 0  | ( 0)          |
|             | pleural fluid   | 2                               | : (4)        | 0 ( 0)         | ) 1  | (2)           | 3  | (6)           |
|             | ascites         | 0                               | ( 0)         | 0 ( 0)         | ) 0  | ( 0)          | 1  | (2)           |
| other       | ear:nodule      | 2                               | : ( 4)       | 0 ( 0          | ) 0  | ( 0)          | 0  | ( 0)          |
|             | hindlimb:nodule | 0                               | ) ( 0)       | 0 ( 0          | ) 0  | ( 0)          | 1  | (2)           |
|             | nose:elevated   | 0                               | ) ( 0)       | 0 ( 0          | ) 0  | ( 0)          | 6  | (12)          |
|             | nose:nodule     | 0                               | ) ( 0)       | 0 ( 0          | )) 0 | ( 0)          | 1  | (2)           |
| whole body  | anemic          | C                               | ) ( 0)       | 1 ( 2          | 2) 1 | (2)           | 0  | ( 0)          |

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(HPT080)

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APPENDIX G 2

GROSS FINDINGS : SUMMARY, RAT : MALE

DEAD AND MORIBUND ANIMALS

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

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| Organ       | Findings    | Group Name 0 ppm<br>NO. of Animals 10 (%) |   | 3 ppm<br>(%) 12 | 10 ppm<br>(%) 27 | 30 ppm<br>7 (%) |
|-------------|-------------|-------------------------------------------|---|-----------------|------------------|-----------------|
|             |             |                                           |   | ( )             | (                |                 |
| skin/app    | nodule      | 0 ( 0)                                    |   |                 |                  | 5 (19)          |
| subcutis    | edema       | 0 ( 0)                                    | 0 | ( 0) 1          | (8) (            | ) ( 0)          |
|             | jaundice    | 0 ( 0)                                    | 0 | ( 0) 0          | ( 0)             | (4)             |
|             | mess        | 3 (30)                                    | 1 | (13) 4          | (33)             | 5 (19)          |
| lung        | red         | 1 (10)                                    | 0 | ( 0) · 0        | ( 0)             | L (4)           |
|             | white zone  | 0 ( 0)                                    | 0 | ( 0) 1          | (8)              | ) ( 0)          |
|             | red zone    | 0 ( 0)                                    | 0 | ( 0) 0          | ( 0)             | L ( 4)          |
|             | yellow zone | 0 ( 0)                                    | 1 | (13) 0          | ) ( 0) (         | ) ( 0)          |
|             | red patch   | 0 ( 0)                                    | 1 | (13) 0          | ) ( 0)           | 1 ( 4)          |
|             | nodule      | 0 ( 0)                                    | 1 | (13) 0          | ) ( 0)           | 0)              |
|             | voluminus   | 0 ( 0)                                    | 0 | ( 0) 0          | ) ( 0)           | 1 (4)           |
| lymph node  | enlarged    | 2 (20)                                    | 0 | ( 0) 0          | ) ( 0)           | 1 (4)           |
| spleen      | enlarged    | 7 (70)                                    | 2 | (25) 2          | 2 (17)           | 3 (11)          |
|             | white zone  | 0 ( 0)                                    | 0 | ( 0) 1          | (8)              | 0 ( 0)          |
|             | nodule      | 0 ( 0)                                    | 0 | ( 0) 0          | ) ( 0)           | 1 (4)           |
| heart       | white zone  | 0 ( 0)                                    | 0 | ( 0) 1          | (8)              | 0 ( 0)          |
|             | fluid:red   | 0 ( 0)                                    | 0 | ( 0) (          | ) ( 0)           | 1 (4)           |
|             | fluid:brown | 0 ( 0)                                    | 0 | ( 0) (          | ) ( 0)           | 1 ( 4)          |
| salivary gl | nodule      | 0 ( 0)                                    | 0 | ( 0) 1          | L ( 8)           | 0 ( 0)          |
| forestomach | nodule      | 0 ( 0)                                    | 0 | ( 0) 1          | L ( 8)           | 0 ( 0)          |
|             | ulcer       | 1 (10)                                    | 0 | (0)             | ) ( 0)           | 1 (4)           |
| gl stomach  | black zone  | 0 ( 0)                                    | 0 | ( 0)            | ) ( 0)           | 1 (4)           |

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

| )rgan       | Findings               | Group Name 0 ppm<br>NO. of Animals 10 (%) | 3 ppm<br>8 (%) | 10 ppm<br>12 (%) | 30 ppm<br>27 (%) |
|-------------|------------------------|-------------------------------------------|----------------|------------------|------------------|
| gl stomach  | ulcer                  | 0 ( 0)                                    | 0 ( 0)         | 0 ( 0)           | 1 (4)            |
|             | erosion                | 1 (10)                                    | 0 ( 0)         | 0 ( 0)           | 0 ( 0)           |
| small intes | red zone               | 0 ( 0)                                    | 0 ( 0)         | 0 ( 0)           | 1 ( 4)           |
| liver       | enlarged               | 0 ( 0)                                    | 0 ( 0)         | 1 ( 8)           | 0 ( 0)           |
|             | pale                   | 1 (10)                                    | 0 ( 0)         | 0 ( 0)           | 0 ( 0)           |
|             | nodule                 | 0 ( 0)                                    | 1 (13)         | 0 ( 0)           | 0 ( 0)           |
|             | rough                  | 1 (10)                                    | 0 ( 0)         | 1 ( 8)           | 0 ( 0)           |
|             | herniation             | 0 ( 0)                                    | 3 (38)         | 0 ( 0)           | 3 (11)           |
| idney       | enlarged               | 0 ( 0)                                    | 0 ( 0)         | 0 ( 0)           | 1 ( 4)           |
|             | cyst                   | 0 ( 0)                                    | 0 ( 0)         | 0 ( 0)           | 1 (4)            |
|             | granular               | 1 (10)                                    | 0 ( 0)         | 2 (17)           | 1 (4)            |
| urin bladd  | urine:marked retention | 1 (10)                                    | 0 ( 0)         | 0 ( 0)           | 1 (4)            |
| pituitary   | enlarged               | 1 (10)                                    | 0 ( 0)         | 0 ( 0)           | 2 (7)            |
|             | nodule                 | 1 (10)                                    | 1 (13)         | 1 ( 8)           | 1 (4)            |
| thyroid     | enlarged               | 0 ( 0)                                    | 0 ( 0)         | 0 ( 0)           | 1 (4)            |
| drensl      | enlarged               | 0 ( 0)                                    | 1 (13)         | 1 ( 8)           | 1 ( 4)           |
| testis      | atrophic               | 0 ( 0)                                    | 0 ( 0)         | 2 (17)           | 1 (4)            |
|             | nodule                 | 3 (30)                                    | 2 (25)         | 8 (67)           | 23 (85)          |
| brain       | red zone               | 0 ( 0)                                    | 0 ( 0)         | 1 ( 8)           | 1 (4)            |
|             | hemorrhage             | 0 ( 0)                                    | 1 (13)         | 0 ( 0)           | 0 ( 0)           |
|             | deformed               | 0 ( 0)                                    | 0 ( 0)         | 0 ( 0)           | 1 (4)            |
| pinal cord  | hemorrhage             | 0 ( 0)                                    | 1 (13)         | 0 ( 0)           | 0 ( 0)           |

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

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| Organ       | Findings        | Group Name<br>NO. of Animals | 0 ppm<br>10 (%) | 3 ppm<br>8 (%) | 10 ppm<br>12 (%) | 30 ppm<br>27 (%)                       |
|-------------|-----------------|------------------------------|-----------------|----------------|------------------|----------------------------------------|
|             |                 |                              |                 |                |                  | ······································ |
| eye         | turbid          |                              | 0 ( 0)          | 0 ( 0)         | 0 ( 0)           | 1 ( 4)                                 |
|             | white           |                              | 0 ( 0)          | 0 ( 0)         | 0 ( 0)           | 2 (7)                                  |
| Zymbal gl   | nodule          |                              | 0 ( 0)          | 1 (13)         | 1 ( 8)           | 1 (4)                                  |
| muscle      | nodule          |                              | 0 ( 0)          | 0 ( 0)         | 1 ( 8)           | 0 ( 0)                                 |
| bone        | nodule          |                              | 0 ( 0)          | 1 (13)         | 0 ( 0)           | 0 ( 0)                                 |
| peritoneum  | nodule          |                              | 0 ( 0)          | 1 (13)         | 2 (17)           | 13 (48)                                |
|             | thick           |                              | 0 ( 0)          | 0 ( 0)         | 0 ( 0)           | 1 ( 4)                                 |
| retroperit  | mass            |                              | 0 ( 0)          | 0 ( 0)         | 0 ( 0)           | 1 (4)                                  |
| abdominal c | hemorrhage      |                              | 0 ( 0)          | 0 ( 0)         | 1 ( 8)           | 0 ( 0)                                 |
|             | pleural fluid   |                              | 0 ( 0)          | 0 ( 0)         | 0 ( 0)           | 1 ( 4)                                 |
|             | ascites         |                              | 1 (10)          | 0 ( 0)         | 2 (17)           | 10 (37)                                |
| mesenterium | mass            |                              | 1 (10)          | 0 ( 0)         | 0 ( 0)           | 0 ( 0)                                 |
| thoracic ca | hemorrhage      |                              | 0 ( 0)          | 0 ( 0)         | 1 ( 8)           | 0 ( 0)                                 |
|             | nodule          |                              | 0 ( 0)          | 0 ( 0)         | 1 ( 8)           | 0 ( 0)                                 |
|             | pleural fluid   |                              | 0 ( 0)          | 0 ( 0)         | 1 ( 8)           | 3 (11)                                 |
|             | ascites         |                              | 0 ( 0)          | 0 ( 0)         | 0 ( 0)           | 1 ( 4)                                 |
| other       | ear:nodule      |                              | 1 (10)          | 0 ( 0)         | 0 ( 0)           | 0 ( 0)                                 |
|             | hindlimb:nodule |                              | 0 ( 0)          | 0 ( 0)         | 0 ( 0)           | 1 ( 4)                                 |
|             | nose:elevated   |                              | 0 ( 0)          | 0 ( 0)         | 0 ( 0)           | 3 (11)                                 |
|             | nose:nodule     |                              | 0 ( 0)          | 0 ( 0)         | 0 ( 0)           | 1 ( 4)                                 |
| whole body  | anemic          |                              | 0 ( 0)          | 0 ( 0)         | 1 ( 8)           | 0 ( 0)                                 |

APPENDIX G 3

GROSS FINDINGS : SUMMARY, RAT : MALE

SACRIFICED ANIMALS

#### STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

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

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| 38h      | Findings   | Group Name 0 ppm<br>NO. of Animals 40 (%) | 3 ppm<br>42 (%) | 10 ppm<br>38 (%) | 30 ppm<br>23 (%) |
|----------|------------|-------------------------------------------|-----------------|------------------|------------------|
| in∕app   | nodule     | 3 ( 8)                                    | 4 (10)          | 3 ( 8)           | 7 (30)           |
|          | scab       | 0 ( 0)                                    | 1 (2)           | 0 ( 0)           | 0 ( 0)           |
| cutis    | nodule     | 1 ( 3)                                    | 0 ( 0)          | 0 ( 0)           | 0 ( 0)           |
|          | mass       | 7 (18)                                    | 7 (17)          | 7 (18)           | 9 (39)           |
| g        | white zone | 0 ( 0)                                    | 1 (2)           | 3 ( 8)           | 2 (9)            |
|          | nodule     | 5 (13)                                    | 1 (2)           | 0 ( 0)           | 0 ( 0)           |
| een      | enlarged   | 2 ( 5)                                    | 1 (2)           | 1 ( 3)           | 1 ( 4)           |
|          | white zone | 0 ( 0)                                    | 0 ( 0)          | 0 ( 0)           | 1 (4)            |
|          | deformed   | 0 ( 0)                                    | 1 (2)           | 0 ( 0)           | 0 ( 0)           |
| ivary gl | nodule     | 0 ( 0)                                    | 0 ( 0)          | 1 ( 3)           | 0 ( 0)           |
| mach     | nodule     | 0 ( 0)                                    | 1 (2)           | 0 ( 0)           | 0 ( 0)           |
| ll intes | nodule     | 0 ( 0)                                    | 0 ( 0)          | 0 ( 0)           | 1 ( 4)           |
| er       | nodule     | 1 ( 3)                                    | 2 ( 5)          | 1 ( 3)           | 0 ( 0)           |
|          | rough      | 4 (10)                                    | 1 ( 2)          | 1 ( 3)           | 3 (13)           |
|          | herniation | 5 (13)                                    | 6 (14)          | 6 (16)           | 0 ( 0)           |
| creas    | nodule     | 2 ( 5)                                    | 0 ( 0)          | 0 ( 0)           | 0 ( 0)           |
| lney     | granular   | 17 (43)                                   | 19 (45)         | 18 (47)          | 15 (65)          |
| n bladd  | nodule     | 0 ( 0)                                    | 0 ( 0)          | 0 ( 0)           | 1 ( 4)           |
| uitary   | enlarged   | 1 ( 3)                                    | 4 (10)          | 1 ( 3)           | 2 (9)            |
|          | red zone   | 3 ( 8)                                    | 3 (7)           | 3 ( 8)           | 1 (4)            |
|          | nodule     | 3 ( 8)                                    | 4 (10)          | 2 (5)            | 6 (26)           |
| roid     | enlarged   | 3 ( 8)                                    | 2 ( 5)          | 2 ( 5)           | 5 (22)           |

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STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

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

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PAGE : 2

arged rophic Hule rbid		0	(3)	0	( 0)		( 3)	0	( 0)
rophic Mule		0					(3)	0	( 0)
lule			( 0)	0	( 0)				
		35			( 0)	1	(3)	0	( 0)
bid			(88)	37	(88)	33	(87)	21	(91)
		0	( 0)	0	( 0)	0	( 0)	1	( 4)
te		3	(8)	0	( 0)	1	(3)	0	( 0)
i		0	( 0)	0	( 0)	0	( 0)	1	( 4)
lule		0	( 0)	0	( 0)	0	( 0)	1	( 4)
dule		0	( 0)	2	(5)	0	( 0)	1	(4)
lule		2	(5)	4	(10)	7	(18)	5	(22)
35		0	( 0)	0	( 0)	1	(3)	0	( 0)
st		0	( 0)	0	( 0)	1	(3)	0	( 0)
zites		0	( 0)	1	(2)	3	(8)	1	(4)
eural fluid		2	(5)	0	( 0)	0	( 0)	0	( 0)
r:nodule		1	(3)	0	( 0)	0	(0)		(0)
se:elevated		0	( 0)	0	( 0)				(13)
emic		0	( 0)			0	(0)		( 0)
l lu lu lu ss t st se	le le tes ral fluid nodule :elevated	le le tes rel fluid nodule :elevated	le 0	1e       0       (       0)         1e       0       (       0)         1e       2       (       5)         1e       2       (       5)         1e       0       (       0)         1e       2       (       5)         1e       2       (       5)         1e       2       (       5)         1e       1       (       3)         1e       1       (       3)         1e       1       1       1	1e       0       (       0)       0         1e       0       (       0)       2         1e       0       (       0)       2         1e       2       (       5)       4         0       (       0)       0       0         1e       2       (       5)       4         0       (       0)       0       0         1e       2       (       5)       4         0       (       0)       0       0         tes       0       (       0)       1         ral fluid       2       (       5)       0         nodule       1       (       3)       0	1e       0       (       0)       0       (       0)         1e       0       (       0)       0       (       0)         1e       2       (       5)       4       (       10)         1e       2       (       5)       0       (       0)         tes       0       (       0)       1       (       2)         ral fluid       1       (       3)       0       (       0)         ielevated       0       (       0)       0       (       0)       0       (       0)	1       0       1       0       1       0       1       0       1       0       1       0	$ \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 &$	1       1

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APPENDIX G 4

GROSS FINDINGS : SUMMARY, RAT : FEMALE

ALL ANIMALS

#### STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

SEX : FEMALE

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

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Organ	Findings	Group Name NO. of Animals	50	0 ppm (%)	50	3 ppm (%)	49	10 ppm (%)	50	30 ppm (%)
skin/app	nodule		1	(2)	0	( 0)	2	(4)	4	(8)
	scab		0	( 0)	0	( 0)	0	( 0)	1	(2)
subcutis	jaundice		1	(2)	0	( 0)	1	(2)	1	(2)
	nodule		0	( 0)	0	( 0)	1	(2)	0	( 0)
	mass		9	(18)	9	(18)	19	( 39)	20	( 40)
lung	red		0	( 0)	1	(2)	0	( 0)	0	( 0)
	white zone		0	( 0)	2	( 4)	2	( 4)	1	(2)
	red zone		0	( 0)	1	(2)	0	( 0)	2	( 4)
	brown zone		1	(2)	0	( 0)	0	( 0)	0	( 0)
	nodule		0	( 0)	0	( 0)	2	(4)	1	(2)
lymph node	enlarged		0	( 0)	0	( 0)	2	( 4)	2	( 4)
spleen	enlarged		4	(8)	5	( 10)	2	( 4)	9	(18)
	nodule		0	( 0)	0	( 0)	1	(2)	1	(2)
heart	white zone		0	( 0)	0	( 0)	0	( 0)	1	(2)
oral cavity	nodule		0	( 0)	0	( 0)	1	(2)	0	( 0)
tongue	nodule		0	( 0)	1	(2)	1	(2)	1	(2)
gl stomach	nodule		0	( 0)	0	( 0)	1	(2)	0	( 0)
	ulcer		0	( 0)	2	( 4)	0	( 0)	0	( 0)
small intes	nodule		0	( 0)	0	( 0)	0	( 0)	1	(2)
	dilated		1	(2)	0	( 0)	0	( 0)	0	( 0)
cecum	nodule		0	( 0)	0	( 0)	0	( 0)	1	(2)
liver	white zone		2	( 4)	2	( 4)	1	(2)	0	( 0)

#### STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

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

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Organ	Findings	Group Name NO. of Animals	0 ppm 50 (%)	n 3 ppm 50 (%)	10 ppm 49 (%)	30 ppm 50 (%)
liver	red zone		1 (2)	0 ( 0)	4 (8)	0 ( 0)
	nodule		1 (2)	0 ( 0)	0 ( 0)	1 (2)
	rough		2 (4)	3 (6)	1 (2)	2 (4)
	granular		0 ( 0)	0 ( 0)	0 ( 0)	1 (2)
	nodular		0 ( 0)	1 ( 2)	1 (2)	0 ( 0)
	herniation		15 (30)	4 (8)	14 (29)	4 ( 8)
pancreas	nodule		1 (2)	1 (2)	0 ( 0)	0 ( 0)
kidney	white zone		0 ( 0)	0 ( 0)	0 ( 0)	3 (6)
	nodule		0 ( 0)	1 ( 2)	1 ( 2)	0 ( 0)
	cyst		0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)
	granular		0 ( 0)	3 (6)	1 ( 2)	3 ( 6)
urin bladd	nodule		0 ( 0)	0 ( 0)	1 (2)	0 ( 0)
	urine:marked retention		0 ( 0)	0 ( 0)	1 (2)	1 ( 2)
pituitary	enlarged		7 (14)	8 (16)	5 (10)	3 (6)
	red zone		4 (8)	5 (10)	8 (16)	7 (14)
	black zone		0 ( 0)	0 ( 0)	0 ( 0)	1 (2)
	nodule		9 (18)	7 (14)	8 (16)	5 (10)
thyreid	enlarged		1 (2)	0 ( 0)	1 ( 2)	3 (6)
	nodule		1 (2)	0 ( 0)	0 ( 0)	1 (2)
adrenal	enlarged		1 (2)	2 ( 4)	1 (2)	0 ( 0)
	adhesion		0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)
ovary	enlarged		0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)

#### STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

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

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rgan	Findings	Group Name 0 ppm NO. of Animals 50 (%)	3 ppm 50 (%)	10 ppm 49 (%)	30 ppm 50 (%)
					· · · · · ·
wary	nodule	0 ( 0)	0 ( 0)	0 ( 0)	1 (2)
	cyst	1 (2)	3 (6)	2 ( 4)	1 ( 2)
terus	enlarged	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)
	nodule	5 (10)	10 (20)	13 (27)	11 (22)
	cyst	1 ( 2)	1 ( 2)	1 ( 2)	2 ( 4)
agina	fluid:red	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)
orain	swollen	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)
eve	turbid	1 (2)	0 ( 0)	1 ( 2)	0 ( 0)
	white	3 (6)	2 ( 4)	1 (2)	0 ( 0)
ymbal gl	nodule	0 ( 0)	0 ( 0)	1 (2)	0 ( 0)
oone	nodule	0 ( 0)	0 ( 0)	0 ( 0)	1 (2)
articulus	swollen	0 ( 0)	0 ( 0)	1 (2)	0 ( 0)
ediastinum	mass	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)
peritoneum	nodule	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)
	thick	0 ( 0)	0 ( 0)	0 ( 0)	1 (2)
bdominal c	hemorrhage	0 ( 0)	2 (4)	0 ( 0)	0 ( 0)
	mass	0 ( 0)	0 ( 0)	0 ( 0)	2 (4)
	ascites	0 ( 0)	0 ( 0)	0 ( 0)	2 (4)
horacic ca	hemorrhage	1 (2)	0 ( 0)	0 ( 0)	1 (2)
	pleural fluid	0 ( 0)	0 ( 0)	0 ( 0)	2 (4)
ther	ear:nodule	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)
	nose:elevated	0 ( 0)	0 ( 0)	0 ( 0)	1 (2)

STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE	GROSS FINDINGS (SUMMARY) ALL ANIMALS (0-105W)				PAGE : 8
Organ Findings	Group Name NO. of Animals	0 ppm 50 (%)	3 ppm 50 (%)	10 ppm 49 (%)	30 ppm 50 (%)
whole body anemic		0 ( 0)	0 ( 0)	0 ( 0)	1 (2)
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APPENDIX G 5

GROSS FINDINGS : SUMMARY, RAT : FEMALE

DEAD AND MORIBUND ANIMALS

STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj : FEMALE

REPORT TYPE : A1

SEX

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

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gan	Findings	Group Name NO. of Animals	0 ppm 9 (%)	3 ppm 12 (%)	10 ppm 10 (%)	30 18 (%	) ppm %)
in/app	nodule		0 ( 0)	0 ( 0)	0 ( 0)	2 (1	11)
bcutis	jaundice		1 (11)	0 ( 0)	1 (10)	1 (	6)
	mass		1 (11)	2 (17)	4 (40)	4 (2	22)
Ig	red		0 ( 0)	1 ( 8)	0 ( 0)	0 (	0)
	red zone		0 ( 0)	1 ( 8)	0 ( 0)	1 (	6)
	nodule		0 ( 0)	0 ( 0)	1 (10)	1 (	6)
mph node	enlarged		0 ( 0)	0 ( 0)	2 (20)	1 (	6)
leen	enlarged		2 (22)	4 (33)	2 (20)	6 (:	33)
	nodule		0 ( 0)	0 ( 0)	0 ( 0)	1 (	6)
rt	white zone		0 ( 0)	0 ( 0)	0 ( 0)	1 (	6)
igue	nodule		0 ( 0)	0 ( 0)	0 ( 0)	1 (	6)
stomach	ulcer		0 ( 0)	1 ( 8)	0 ( 0)	0 (	0)
ver	red Zone		0 ( 0)	0 ( 0)	1 (10)	0 (	0)
	nodule		0 ( 0)	0 ( 0)	0 ( 0)	1 (	6)
	rough		1 (11)	2 (17)	0 ( 0)	0 (	0)
	granular		0 ( 0)	0 ( 0)	0 ( 0)	1 (	6)
	herniation		1 (11)	1 ( 8)	5 (50)	1 (	6)
ncreas	nodule		1 (11)	1 ( 8)	0 ( 0)	0 (	0)
lney	white zone		0 ( 0)	0 ( 0)	0 ( 0)	1 (	6)
	nodule		0 ( 0)	0 ( 0)	1 (10)	0 (	0)
n <sub>.</sub> bladd	urine:marked retention		0 ( 0)	0 ( 0)	1 (10)	1 (	6)
uitary	enlarged		3 (33)	4 (33)	2 (20)	2 (	11)

PAGE : 4

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#### STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

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

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Drgan	Findings	Group Name 0 _ NO. of Animals 9 (?	ppm 3 ppm 6) 12 (%)	10 ppm 10 (%)	18	30 ppm (%)
ituitary	red zone	0 (		1 (10)		(6)
	black zone	0 (	0) 0 ( 0)	0 ( 0)	1	(6)
	nodule	2 (	22) 0 ( 0)	0 ( 0)	0	( 0)
hyroid	enlarged	0 (	0) 0 ( 0)	0 ( 0)	1	(6)
	nodule	0 (	0) 0 ( 0)	0 ( 0)	1	(6)
drenal	enlarged	0 (	0) 1 ( 8)	1 (10)	0	( 0)
	adhesion	0 (	0) 0 ( 0)	1 (10)	0	( 0)
vary	enlarged	0 (	0) 1 ( 8)	0 ( 0)	0	( 0)
	nodule	0 (	0) 0 ( 0)	0 ( 0)	1	(6)
	cyst	0 (	0) 1 ( 8)	0 ( 0)	0	(0)
terus	enlarged	0 (	0) 1 ( 8)	0 ( 0)	0	(0)
	nodule	1 (	11) 3 (25)	4 (40)	7	(39)
	cyst	0 (	0) 0 ( 0)	0 ( 0)	1	(6)
agina	fluid:red	0 (	0) 0 ( 0)	0 ( 0)	t	(6)
rain	swollen	0 (	0) 0 ( 0)	1 (10)	0	(0)
ymbal gl	nodule	0 (	0) 0 ( 0)	1 (10)		(0)
rticulus	swollen	0 (		1 (10)		(0)
ediastinum	mass	1 (		0 ( 0)		( 0)
eritoneum	thick	0 (		0 ( 0)		(6)
bdominal c	hemorrhage	0 (		0 ( 0)		( 0)
	mass	0 (		0 ( 0)		(11)
	ascites	0 (		0 ( 0)	2	(11)

#### STUDY NO. : 0342 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	0 ppm 9 (%)	3 ppm 12 (%)	10	10 ppm (%)	18	30 ppm (%)
thoracic ca	hemorrhage		1 (11)	0 ( 0)	0	(0)	0	( 0)
	pleural fluid		0 ( 0)	0 ( 0)	0	( 0)	1	(6)
other	ear:nodule		0 ( 0)	0 ( 0)	0	( 0)	1	(6)
	nose:elevated		0 ( 0)	0 ( 0)	0	( 0)	1	(6)
whole body	anemic		0 ( 0)	0 ( 0)	0	(0)	1	(6)

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APPENDIX G 6

GROSS FINDINGS : SUMMARY, RAT : FEMALE

SACRIFICED ANIMALS

STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE

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

Organ	Findings	Group Name NO. of Animals	0 ppr 41 (%)	n 3 ppm 38 (%)	10 ppm 39 (%)	32	30 ppm (%)
skin/app	nodule		1 (2)	0 ( 0)	2 (5)	2	( 6)
	scab		0 ( 0)	0 ( 0)	0 ( 0)	1	(3)
subcutis	nodule		0 ( 0)	0 ( 0)	1 ( 3)	0	( 0)
	mass		8 (20)	7 (18)	15 (38)	16	(50)
lung	white zone		0 ( 0)	2 ( 5)	2 (5)	1	(3)
	red zone		0 ( 0)	0 ( 0)	0 ( 0)	1	(3)
	brown zone		1 (2)	0 ( 0)	0 ( 0)	0	( 0)
	nodule		0 ( 0)	0 ( 0)	1 ( 3)	0	( 0)
lymph node	enlarged		0 ( 0)	0 ( 0)	0 ( 0)	1	(3)
spleen	enlarged		2 (5)	1 ( 3)	0 ( 0)	3	(9)
	nodule		0 ( 0)	0 ( 0)	1 ( 3)	0	( 0)
oral cavity	nodule		0 ( 0)	0 ( 0)	1 (3)	0	( 0)
tongue	nodule		0 ( 0)	1 ( 3)	1 ( 3)	0	( 0)
gl stomach	nodule		0 ( 0)	0 ( 0)	1 (3)	0	( 0)
	ulcer		0 ( 0)	1 ( 3)	0 ( 0)	0	( 0)
small intes	nodule		0 ( 0)	0 ( 0)	0 ( 0)	1	(3)
	dilated		1 (2)	0 ( 0)	0 ( 0)	0	( 0)
cecum	nodule		0 ( 0)	0 ( 0)	0 ( 0)	1	(3)
liver	white zone		2 (5)	2 (5)	1 ( 3)	0	( 0)
	red zone		1 (2)	0 ( 0)	3 (8)	0	( 0)
	nodule		1 (2)	0 ( 0)	0 ( 0)	0	( 0)
	rough		1 (2)	1 ( 3)	1 ( 3)	2	(6)

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#### STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

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

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SEX : FEMALE

| gan      | Findings      | Group Name<br>NO. of Animals | 41 ( | 0 ppm<br>(%) | 38 | 3 ppm<br>(%) | 39 | 10 ppm<br>(%) | 32 | 30 ppm<br>(%) |
|----------|---------------|------------------------------|------|--------------|----|--------------|----|---------------|----|---------------|
| ver      | nodular       |                              | 0 (  | ( 0)         | 1  | (3)          | 1  | ( )           |    | ( 0)          |
|          | herniation    |                              | 14 ( |              |    | (8)          |    | (3)<br>(23)   |    | (0)<br>(9)    |
| dney     | white zone    |                              |      | ( 0)         |    | ( 0)         |    | ( 0)          |    | (6)           |
|          | nodule        |                              |      | (0)          |    | (3)          |    | ( 0)          |    | ( 0)          |
|          | cyst          |                              |      | (0)          |    | (3)          |    | ( 0)          |    | ( 0)          |
|          | granular      |                              |      | ( 0)         |    | (8)          |    | (3)           |    | (9)           |
| in bladd | nodule        |                              |      | (0)          |    | ( 0)         |    | (3)           |    | ( 0)          |
| tuitary  | enlarged      |                              | 4 (  | (10)         | 4  | (11)         |    | (8)           |    | (3)           |
|          | red zone      |                              | 4 (  | (10)         | 5  | (13)         | 7  | (18)          |    | (19)          |
|          | nodule        |                              | 7 (  | (17)         | 7  | (18)         | 8  | (21)          | 5  | (16)          |
| roid     | enlarged      |                              | 1 (  | (2)          | 0  | ( 0)         | 1  | (3)           | 2  | (6)           |
|          | nodule        |                              | 1 (  | (2)          | 0  | ( 0)         | 0  | ( 0)          | 0  | ( 0)          |
| renal    | enlarged      |                              | 1 (  | (2)          | 1  | (3)          | 0  | ( 0)          | 0  | ( 0)          |
| ary      | cyst          |                              | 1 (  | (2)          | 2  | (5)          | 2  | (5)           | 1  | (3)           |
| erus     | nodule        |                              | 4    | (10)         | 7  | (18)         | 9  | (23)          | 4  | (13)          |
|          | cyst          |                              | 1 (  | (2)          | 1  | (3)          | 1  | (3)           | 1  | (3)           |
| 9        | turbid        |                              | 1 (  | (2)          | 0  | ( 0)         | 1  | (3)           | 0  | ( 0)          |
|          | white         |                              | 3 (  | (7)          | 2  | (5)          | 1  | (3)           | 0  | ( 0)          |
| le       | nodule        |                              | 0    | ( 0)         | 0  | ( 0)         | 0  | ( 0)          | 1  | (3)           |
| itoneum  | nodule        |                              | 0    | (0)          | 0  | ( 0)         | 1  | (3)           | 0  | ( 0)          |
| racic ca | hemorrhage    |                              | 0    | ( 0)         | 0  | ( 0)         | 0  | ( 0)          | 1  | (3)           |
|          | pleural fluid |                              | 0    | ( 0)         | 0  | ( 0)         | 0  | ( 0)          | 1  | (3)           |

APPENDIX H 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE UNIT: g

NO. of

Group Name

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

TESTES

HEART

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ADRENALS

Body Weight

LUNGS KIDNEYS

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|        | Animals |              |              | 100100       |              | LUNUS        |                   |
|--------|---------|--------------|--------------|--------------|--------------|--------------|-------------------|
| 0 ppm  | 40      | 376± 50      | 0.081± 0.024 | 3.360± 1.462 | 1.167± 0.098 | 1.421± 0.171 | $2.680 \pm 0.224$ |
| 3 ppm  | 42      | 384± 52      | 0.078± 0.013 | 3.577± 1.744 | 1.190± 0.107 | 1.391± 0.104 | 2.701± 0.240      |
| 10 ppm | 38      | $365 \pm 48$ | 0.079± 0.015 | 4.051± 1.426 | 1.179± 0.121 | 1.400± 0.135 | 2.681± 0.275      |
| 30 ppm | 23      | 313± 36**    | 0.076± 0.011 | 4.043± 1.752 | 1.177± 0.110 | 1.493± 0.306 | $2.779 \pm 0.365$ |

(HCL040)

BAIS 3

| oup Name | NO. of<br>Animals | SPLI        | EEN    | LIVI         | ER     | BRA        |     |
|----------|-------------------|-------------|--------|--------------|--------|------------|-----|
| 0 ppm    | 40                | 1.041±      | 0.650  | 11.254±      | 2. 244 | $1.955\pm$ | 050 |
| 3 ppm    | 42                | 0.949 $\pm$ | 0.268  | 11.201±      | 1.654  | $1.957\pm$ | 061 |
| 10 ppm   | 38                | 0.913±      | 0. 189 | $10.938\pm$  | 1.569  | $1.940\pm$ | 057 |
| 30 ppm   | 23                | 0.935±      | 0. 458 | $10.865 \pm$ | 1.906  | $1.932\pm$ | 070 |

APPENDIX H 2

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

STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE UNIT: g

ORGAN WEIGHT: ABSOLUTE (SUMMARY)

SURVIVAL ANIMALS (105W)

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PAGE : 3

| roup Name | NO. of<br>Animals | Body Weight | ADRENALS     | OVARIES           | HEART        | LUNGS             | KIDNEYS        |
|-----------|-------------------|-------------|--------------|-------------------|--------------|-------------------|----------------|
| 0 ppm     | 41                | 249± 25     | 0.083± 0.032 | 0.127± 0.020      | 0.834± 0.067 | 1.014± 0.176      | 1.721± 0.112   |
| 3 ppm     | 38                | 251± 22     | 0.107± 0.179 | $0.151 \pm 0.194$ | 0.836± 0.054 | 0.990± 0.071      | 1.797± 0.270   |
| 10 ppm    | 39                | 252± 25     | 0.077± 0.010 | $0.129 \pm 0.054$ | 0.838± 0.061 | 0.978± 0.071      | 1.788± 0.147   |
| 30 ppm    | 32                | 235± 22*    | 0.076± 0.011 | 0.127± 0.048      | 0.854± 0.075 | $1.055 \pm 0.187$ | 1.874± 0.167** |

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(HCL040)

BAIS 3

| NIT: g    |                   |             |        | -          |        |            |        | PAGE : 4 |
|-----------|-------------------|-------------|--------|------------|--------|------------|--------|----------|
| roup Name | NO. of<br>Animals | SPL         | EEN    | LIV        | ER     | BRA        |        |          |
| 0 ppm     | 41                | 0.628 $\pm$ | 0.840  | 6.434±     | 1.080  | 1.792±     | ). 057 |          |
| 3 ppm     | 38                | 0.611±      | 0. 500 | $6.695\pm$ | 0.890  | 1.785±     | ). 057 |          |
| 10 ppm    | 39                | 0.648±      | 0.972  | $6.507\pm$ | 0, 880 | 1.790±     | ). 050 |          |
| 30 ppm    | 32                | $0.836\pm$  | 0.935* | 6.593±     | 0. 933 | $1.797\pm$ | ). 048 |          |

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APPENDIX I 1

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

STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE UNIT: % ORGAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS (105W)

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oup Name	NO. of Animals	Body Weight (g)	ADRENALS	TESTES	HEART	LUNGS	KIDNEYS
0 ppm	40	376± 50	0.022± 0.007	0.917± 0.421	0.313± 0.031	0.381± 0.050	0.720± 0.080
3 ppm	42	$384\pm$ 52	$0.021 \pm 0.004$	0.943± 0.480	0.314± 0.045	0.367± 0.046	0.711± 0.079
10 ppm	38	$365 \pm 48$	0.022± 0.005	1.140± 0.464	0.325± 0.027	0.387± 0.035	0.741± 0.080
30 ppm	23	313± 36**	0.025± 0.006*	1.282± 0.514**	0.382± 0.063**	0.482± 0.107**	0.898± 0.150**

(HCL042)

BAIS 3

STUDY NO. : 034 ANIMAL : RAT REPORT TYPE : A SEX : MALE UNIT: %	F344/DuCrj		ORGAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS (105W)						
Group Name	NO. of Animals	SPLEEN	LIVER	BRAIN	PAGE : 2				
0 ppm	40	0.279± 0.173	3.013± 0.601	0.527± 0.055					
3 ppm	42	$0.250 \pm 0.080$	2.937± 0.403	$0.516 \pm 0.052$					
10 ppm	38	0.255± 0.068	3.009± 0.370	0.539± 0.063					
30 ppm	23	0.298± 0.135	3.488± 0.621**	0.626± 0.084**					
Significant (HCL042)	difference ;	*:P≦0.05 **:	P ≦ 0.01	Test of Dunnett	BAIS 3				

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BAIS 3

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APPENDIX I 2

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

STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE UNIT: % ORGAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS (105W)  $\sim$ 

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oup Name	NO. of Animals	Body	Weight (g)	ADRENALS	OVARIES	HEART	LUNGS	KIDNEYS	
0 ppm	41	249±	25	0.034± 0.020	0.051± 0.009	0.338± 0.033	0.411± 0.074	0.698± 0.067	
3 ppm	38	251±	22	0.045± 0.084	0.061± 0.083	0.335± 0.029	0.397± 0.038	0.723± 0.141	
10 ppm	39	252±	25	0.031± 0.004	$0.052 \pm 0.024$	0.335± 0.024	$0.391 \pm 0.038$	0.713± 0.060	
30 ppm	32	$235\pm$	22*	0.033± 0.005	$0.054 \pm 0.019$	0.366± 0.050**	0.453± 0.100*	0.803± 0.096**	

(HCL042)

BAIS 3

STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : FEMALE UNIT: %

ORGAN WEIGHT: RELATIVE (SUMMARY)

SURVIVAL ANIMALS (105W)

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p Name	NO. of Animals	SPLEEN	LIVER	BRAIN	
0 ppm	41	0.252± 0.326	2.596± 0.392	0.728± 0.079	
3 ppm	38	$0.248 \pm 0.222$	2.683± 0.367	0.717± 0.061	
10 ppm	39	0.255± 0.368	2.583± 0.225	0.717± 0.068	
30 ppm	32	0.362± 0.410*	2.817± 0.423**	$0.771 \pm 0.075*$	

BAIS 3

APPENDIX J 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : ALL ANIMALS

ANIMAL : REPORT TYPE :	0342 RAT F344/DuCrj A1 MALE	HISTOLOGICAL FINDINGS :NON-M ALL ANIMALS (0-105W)	NEOPLASTIC LESIONS (SUMMARY)		
Organ	N	roup Name 0 ppm o. of Animals on Study 50 rade <u>1 2 3 4</u> (%) (%) (%) (%)	3 ppm 50 <u>1 2 3 4</u> (%) (%) (%) (%)	$ \begin{array}{c} 10 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	PAGE : 30  ppm 50 $\frac{1}{50}$ $\frac{1}{50}$ $\frac{3}{50}$ $\frac{1}{50}$ $\frac{1}{50}$ $\frac{3}{50}$ $\frac{1}{50}$ $\frac{3}{50}$ $\frac{1}{50}$ $\frac{1}{50}$ $\frac{3}{50}$ $\frac{1}{50}$
{Integumentar	y system/appandage)				
skin/app	inflammation	<50> 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)	<50> 0 2 0 0 ( 0) ( 4) ( 0) ( 0)
	hyperplasia:epidermis	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)
	scab	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)
	epidermal cyst	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)
Respiratory s	system}				
nasal cavit	thrombus	<50> 0 2 2 0 ( 0) ( 4) ( 4) ( 0)	<50> 1 0 2 0 ( 2) ( 0) ( 4) ( 0)	<50> 2 2 1 0 ( 4) ( 4) ( 2) ( 0)	<50> 1 1 0 0 ( 2) ( 2) ( 0) ( 0)
	mineralization	39 0 0 0 (78) (0) (0) (0)	37 1 0 0 (74) (2) (0) (0)	31 0 0 0 (62)(0)(0)(0)	41 0 0 0 (82) (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 0 0 ( 0) ( 0) ( 0) ( 0)	2 2 0 0 (4)(4)(0)(0)
∑a> b	a : Number of animals examined at the site b : Number of animals with lesion c : b / a * 100				

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# STUDY NO. : 0342

(HPT150)

	N	roup Name 5. of Animals on Study	0 ppm 50	3 ppm 50	10 ppm 50	30 ppm 50
38N	G	rade <u>1</u> (%)	<u>2 3 4</u> (%) (%) (%)	$\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$	$\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$	$\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$
spiratory	system)					
al cavit	eosinophilic change∶olfactory epitheliu		<50> 17 3 0 (34) (6) (0)	<50> 28 15 2 0 (56) (30) (4) (0)	<50> 19 16 5 0 (38) (32) (10) (0)	<50> 33 2 0 0 * (66) (4) (0) (0)
	eosinophilic change:respiratory epithel		1 0 0 (2)(0)(0)	27 0 0 0 (54)(0)(0)(0)	29 0 0 0 (58)(0)(0)(0)	17 1 0 0 (34) (2) (0) (0)
	inflammation:foreign body	17 ( 34)	1 0 0 (2)(0)(0)	17 4 0 0 (34) (8) (0) (0)	15 2 0 0 (30)(4)(0)(0)	11 1 0 0 (22) (2) (0) (0)
	inflammation:squamous epithelium	1 ( 2)	0 0 0 ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	inflammation:respiratory epithelium	7 (14)	0 0 0 ( 0) ( 0) ( 0)	6 0 0 0 (12) (0) (0) (0)	5 1 0 0 (10) (2) (0) (0)	9 23 0 0 (18) (46) (0) (0)
	respiratory metaplasia:olfactory epithe	lium 3 (6)	0 0 0 ( 0) ( 0) ( 0)	3 0 0 0 (6)(0)(0)(0)	2 0 0 0 ( 4) ( 0) ( 0) ( 0)	4 0 0 0 (8)(0)(0)(0)
	respiratory metaplasia:gland	41 ( 82)	0 0 0 ( 0) ( 0) ( 0)	48 0 0 0 (96)(0)(0)(0)	48 0 0 0 (96)(0)(0)(0)	44 0 0 0 (88) (0) (0) (0)
	inflammation:transitional epithelium	9 (18)	0 0 0 ( 0) ( 0) ( 0)	15 0 0 0 (30) (0) (0) (0)	3 0 0 0 (6)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

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b b: Number of anima (c) c: b/a \* 100

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

STUDY NO. : 0342

STUDY NO.	:	0342
ANIMAL	:	RAT F344/DuCrj
REPORT TYPE	;	A1
SEX	;	MALE

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

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MALE																								PAGE	: 3
	No. of Animals on Stu	iy <u>1</u> (%)		i0 3	3	4 (%)		(*	1 %)	2 (%)	50 3		4 (%)	_ <u>1</u> (%	5)					<u>    1</u> (%)	(	50 2		4 (%)	
system)																									
squamous cell metaplasia:respiratory e	pithelium (	1 2)	0	C		0 ( 0)		(	2 4) (	0	0	i) (	0 0)	; ( (	3 3) (	0	0	(	0 0)	( 2)		0	1	0 ( 0)	
squamous cell metaplasia with atypia:r ium		0 0)	0 ( 0)			0 ( 0)				0 0)			0 0)	; ( 10	5 )) (	0 0)	0 ( 0)		0 0)				0 0)		**
squamous cell hyperplasia with atypia	(	0 0)	0 ( 0)			0 ( 0)		(	0 0) (	0 0)	0 ( 0	) )) (	0 0)			0 0)	0 ( 0)	(	0 0)				0 0)		**
hyperplasia with atypia:respiratory ep		0 0)	0 ( 0)			0 ( 0)		(	0 0) (	0 0)	0 ( 0	) )) (	0 0)			0 0)	0 ( 0)	(	0 0)			0 0) (	0 0)	0 ( 0)	
hyperplasia with atypia:nasal gland	(	0 0)	0 ( 0)			0 ( 0)				0 0)			0 0)			0 0)	0 ( 0)	(	0 0)				0 0)	0 ( 0)	
hyperplasia with atypia:transitional e	pithelium (	0 0)	0 ( 0)	( (	0 0) (	0 ( 0)	ł	(	0 0) (	0 0)	( (	) )) (	0 0)	( )	3 6) (	0 0)	0 ( 0)	(	0 0)	4 ( 8	) (		0 0)	0 ( 0)	
hyperplasia:transitional epithelium	(	0 0)	0 ( 0)			0 ( 0)	I			0 0)			0 0)			0 0)	0 ( 0)	(	0 ** 0)			1 2) (	0 ( 0)	0 ( 0)	
atrophy:olfactory epithelium	(	0 0)	0 ( 0)			0 ( 0)				0 ( 0)			0 0)			0 0)	0 ( 0)	• (	0 0)			0 0) (	0 ( 0)		** )
	Findings	Group Name No. of Animals on Stud Grade Findings	Group Name No. of Animals on Study Grade         Findings	$\begin{array}{c} Group Name \\ No. of Animals on Study \\ Grade \\ \hline 1 \\ \hline 2 \\ \hline \\ Grade \\ \hline \\ $	$\begin{array}{c} Group Name & 0 pr \\ No. of Animals on Study & 50 \\ Grade & 1 & 2 & (\%) & (\%) & (9) \\ \hline \\ Findings & (\%) & (\%) & (\%) & (9) \\ \hline \\ system & (50) \\ squamous cell metaplasia:respiratory epithelium & 1 & 0 & (2) \\ (2) & (0) & (1) \\ \hline \\ squamous cell metaplasia with atypia:respiratory epithel & 0 & 0 \\ \hline \\ um & (0) & (0) & (0) \\ \hline \\ squamous cell hyperplasia with atypia \\ \hline \\ squamous cell hyperplasia with atypia \\ \hline \\ (0) & (0) & (0) \\ \hline \\ hyperplasia with atypia:respiratory epithelium \\ \hline \\ (0) & (0) & (0) \\ \hline \\ hyperplasia with atypia:nasal gland \\ \hline \\ (0) & (0) & (0) \\ \hline \\ hyperplasia with atypia:transitional epithelium \\ \hline \\ (0) & (0) & (0) \\ \hline \\ hyperplasia:transitional epithelium \\ \hline \\ \hline \\ (0) & (0) & (0) \\ \hline \\ hyperplasia:transitional epithelium \\ \hline \\ \hline \\ (0) & (0) & (0) \\ \hline \\ hyperplasia:transitional epithelium \\ \hline \\ \hline \\ 0 & 0 \\ \hline \\ hyperplasia:transitional epithelium \\ \hline \\ \hline \\ 0 & 0 \\ \hline \\ hyperplasia:transitional epithelium \\ \hline \\ \hline \\ 0 & 0 \\ \hline \\ hyperplasia:transitional epithelium \\ \hline \\ \hline \\ 0 & 0 \\ \hline \\ hyperplasia:transitional epithelium \\ \hline \\ \hline \\ 0 & 0 \\ \hline \\ hyperplasia:transitional epithelium \\ \hline \\ \hline \\ 0 & 0 \\ \hline \\ \hline \\ hyperplasia:transitional epithelium \\ \hline \\ \hline \\ \hline \\ 0 & 0 \\ \hline \\ \hline \\ hyperplasia:transitional epithelium \\ \hline \\ $	Group Name0 ppmNo. of Animals on Study0 ppmGrade $1$ $2$ $3$ Findings(%)(%)(%)system) $(50)$ squamous cell metaplasia:respiratory epithelium $1$ $0$ $0$ $0$ $(2)$ $(0)$ $(0)$ squamous cell metaplasia with atypia:respiratory epithel $0$ $0$ $0$ $0$ $(0)$ $(0)$ $(0)$ squamous cell hyperplasia with atypia $0$ $0$ $0$ $0$ $(0)$ </td <td>Group Name No. of Animals on Study0 ppm 50Findings<math>1</math><math>2</math><math>3</math><math>4</math>Findings<math>(\\$)</math><math>(\\$)</math><math>(\\$)</math><math>(\\$)</math><math>(\\$)</math>squamous cell metaplasia:respiratory epithelium<math>1</math><math>0</math><math>0</math><math>0</math>squamous cell metaplasia with atypia:respiratory epithel<math>0</math><math>0</math><math>0</math><math>0</math>squamous cell metaplasia with atypia:respiratory epithel<math>0</math><math>0</math><math>0</math><math>0</math>squamous cell hyperplasia with atypia<math>0</math><math>0</math><math>0</math><math>0</math>squamous cell hyperplasia with atypia<math>0</math><math>0</math><math>0</math><math>0</math>hyperplasia with atypia:respiratory epithelium<math>0</math><math>0</math><math>0</math><math>0</math>hyperplasia with atypia:respiratory epithelium<math>0</math><math>0</math><math>0</math><math>0</math>hyperplasia with atypia:respiratory epithelium<math>0</math><math>0</math><math>0</math><math>0</math>hyperplasia with atypia:respiratory epithelium<math>0</math><math>0</math><math>0</math><math>0</math>hyperplasia with atypia:respiratoric epithelium<math>0</math><math>0</math><math>0</math><math>0</math>hyperplasia with atypia:respiratoric epithelium<math>0</math><math>0</math><math>0</math><math>0</math>hyperplasia:transitional epithelium<math>0</math><math>0</math><math>0</math><math>0</math><math>(0)</math><math>(0)</math><math>(0)</math><math>(0)</math><math>(0)</math><math>(0)</math><math>(0)</math>hyperplasia:transitional epithelium<math>0</math><math>0</math><math>0</math><math>(0)</math><math>(0)</math>hyperplasia:transitional epithelium<math>0</math><math>0</math><math>0</math><math>0</math><math>(0)</math><math>(0)</math><math>(0)</math><math>(0)</math><math>(0)</math><math>(0)</math><math>(0)</math></td> <td><math display="block">\begin{array}{c ccccccccccccccccccccccccccccccccccc</math></td> <td><math display="block"> \begin{array}{c ccccccccccccccccccccccccccccccccccc</math></td> <td><math display="block"> \begin{array}{c ccccccccccccccccccccccccccccccccccc</math></td> <td><math display="block">\begin{array}{c ccccccccccccccccccccccccccccccccccc</math></td> <td><math display="block"> \begin{array}{c ccccccccccccccccccccccccccccccccccc</math></td> <td><math display="block"> \begin{array}{c ccccccccccccccccccccccccccccccccccc</math></td> <td><math display="block">\begin{array}{c ccccccccccccccccccccccccccccccccccc</math></td> <td><math display="block">\begin{array}{c ccccccccccccccccccccccccccccccccccc</math></td> <td><math display="block"> \begin{array}{c ccccccccccccccccccccccccccccccccccc</math></td> <td><math display="block"> \begin{array}{c ccccccccccccccccccccccccccccccccccc</math></td> <td><math display="block">\begin{array}{c ccccccccccccccccccccccccccccccccccc</math></td> <td>Group Name No. of Animals on Study         0 ppm         3 ppm         10 ppm           Findings         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         1         0</td> <td><math display="block"> \begin{array}{c ccccccccccccccccccccccccccccccccccc</math></td> <td><math display="block"> \begin{array}{c ccccccccccccccccccccccccccccccccccc</math></td> <td><math display="block">\begin{array}{c ccccccccccccccccccccccccccccccccccc</math></td> <td><math display="block">\begin{array}{c ccccccccccccccccccccccccccccccccccc</math></td> <td><math display="block">\begin{array}{c ccccccccccccccccccccccccccccccccccc</math></td> <td>Group Ness No. of Animals on Study         0 ppm 50         3 ppm 50         3 ppm 50         10 ppm 50         10 ppm 50         30 ppm 50           Findings         (6)</td>	Group Name No. of Animals on Study0 ppm 50Findings $1$ $2$ $3$ $4$ Findings $(\$)$ $(\$)$ $(\$)$ $(\$)$ $(\$)$ squamous cell metaplasia:respiratory epithelium $1$ $0$ $0$ $0$ squamous cell metaplasia with atypia:respiratory epithel $0$ $0$ $0$ $0$ squamous cell metaplasia with atypia:respiratory epithel $0$ $0$ $0$ $0$ squamous cell hyperplasia with atypia $0$ $0$ $0$ $0$ squamous cell hyperplasia with atypia $0$ $0$ $0$ $0$ hyperplasia with atypia:respiratory epithelium $0$ $0$ $0$ $0$ hyperplasia with atypia:respiratoric epithelium $0$ $0$ $0$ $0$ hyperplasia with atypia:respiratoric epithelium $0$ $0$ $0$ $0$ hyperplasia:transitional epithelium $0$ $0$ $0$ $0$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ hyperplasia:transitional epithelium $0$ $0$ $0$ $(0)$ $(0)$ hyperplasia:transitional epithelium $0$ $0$ $0$ $0$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Group Name No. of Animals on Study         0 ppm         3 ppm         10 ppm           Findings         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         2         3         4         1         1         0	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Group Ness No. of Animals on Study         0 ppm 50         3 ppm 50         3 ppm 50         10 ppm 50         10 ppm 50         30 ppm 50           Findings         (6)

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

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

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

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

EPORT TYPE : EX :	MALE					PAGE :
rgan	Findings	Group Name 0 No. of Animals on Study 50 Grade <u>1 2</u> (%) (%)	ppm <u>3 4</u> (%) (%)	3 ppm 50 <u>1 2 3 4</u> (%) (%) (%) (%)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	30 ppm 50 <u>1 2 3 4</u> (%) (%) (%) (%)
Respiratory	system)					
asal cavit	necrosis:olfactory epithelium	<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> 3 0 0 0 ( 6) ( 0) ( 0) ( 0)
	necrosis:respiratory epithelium	0 0 ( 0) ( 0) (	0 0 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (2)(0)(0)(0)	4 2 1 0 (8) (4) (2) (0)
	hyperplasia:respiratory epithelium	0 0 ( 0) ( 0) (	0 0 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	6 1 0 0 <b>*</b> (12) (2) (0) (0)
	thickening of bone:turbinate	0 0 ( 0) ( 0) (	0 0 0) ( 0)	3 0 0 0 (6)(0)(0)(0)	24 14 0 0 ** (48) (28) (0) (0)	15 6 0 0 <b>**</b> (30) (12) (0) (0)
arynx	inflammation	<50 8 0 (16) (0) (	0 0	<50> 5 0 0 0 (10) (0) (0) (0)	<50> 12 0 0 0 (24) (0) (0) (0)	<50> 8 1 0 0 (16) (2) (0) (0)
ung	congestion	0 1 ( 0) ( 2) (	0 0	<50> 0 2 0 0 ( 0) ( 4) ( 0) ( 0)	<50> 1 1 0 0 ( 2) ( 2) ( 0) ( 0)	<50> 0 3 0 0 ( 0) ( 6) ( 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)	0 1 0 0 (0)(2)(0)(0)

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

(HPT150)

REPORT TYPE SEX	: MALE			-																											PA	GE	:
Organ	Findings	Group Name No. of Animals on Stud Grade	ly 	2 (%)	50	ppm <u>3</u> (%)		4(%)	 	<u>1</u> (%)	:		50	ppm <u>3</u> (%)		<u>4</u> (%)	 (9	6)	(	1) 5) 2 %)		pm <u>3</u> %)		<u>4</u> %)		1 (%)			50	ppm 3 (%)		4(%)	,
{Respiratory	system)																																
lung	edema	(	0 0)	0		0		0 0)	(	0 0)	(	1	50> (	0 0)	(	0 0)		1 2)		<5 1 2)		0 0)	(	0 0)	(	0 0)	(	0		0	(	0 0)	
	perivascular inflammation	(	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)		0 0)	(	0 0)	
	accumulation of foamy cells	(	1 2)	0 ( 0)	) (	0 0)	(	0 0)	(	4 8)	(	0 0)	(	0 0)	(	0 0)	(	4 8)	(	0 0)	(	0 0)	(	0 0)	(	4 8)	(	0 0)	) (	0 0)	(	0 0)	
	bronchiolar-alveolar cell hyperplasia	· (	0 0)	1		0 0)		0 0)	(	2 4)	(	0 0)	(	0 0)	(	0 0)	(	1 2)	(	2 4)	(	0 0)	(	0 0)	(	3 6)	(	3 6)	) (	0 0)	(	0 0)	ļ.
	inflammation:foreign body	(	0 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 2)	) (	0 0)		0 0)	
	hyperplasia:terminal bronchiole	(	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)		0 0)	,

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(Hematopoietic system)

bone marrow	<50>	<50>	<50>	<50>
angiectasis	0 0 0 0	0 0 0 0	1 1 0 0	0 0 0 0
	( 0) ( 0) ( 0) ( 0)	( 0) ( 0) ( 0) ( 0)	(2)(2)(0)(0)	( 0) ( 0) ( 0) ( 0)

Grade	1 : Slight	2 : Moderate	3 : Marked	4 : Severe
<a>&gt;</a>	a : Number of	animals examined at	the site	
b	b : Number of	animals with lesion		
(c)	c:b/a*10	0		
C2 1 C2	1:00			

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

#### STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

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

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| an          | Findings                 | Group Name         0 ppm           No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%) | 3 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
|-------------|--------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|-------------------------------------------------------|-------------------------------------------------------|
| matopoietio | c system)                |                                                                                                                                                                                 |                                                  |                                                       |                                                       |
| e marrow    | 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>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <50><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                |
|             | granulation              | 7 0 0 0<br>(14) (0) (0) (0)                                                                                                                                                     | 3 0 0 0<br>(6)(0)(0)(0)                          | 2 1 0 0<br>(4)(2)(0)(0)                               | 1 0 0 0<br>(2)(0)(0)(0)(0)                            |
|             | proliferation:histiocyte | 0 0 1 0<br>( 0) ( 0) ( 2) ( 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)                        |
|             | increased hematopoiesis  | 5 0 0 0<br>(10) (0) (0) (0)                                                                                                                                                     | 2 0 0 0<br>(4)(0)(0)(0)                          | 3 0 0 0<br>(6)(0)(0)(0)                               | 4 0 0 0<br>(8)(0)(0)(0)                               |
|             | decreased hematopoiesis  | 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)                               | 1 0 0 0<br>(2)(0)(0)(0)                               |
|             | erythropoiesis:increased | 0 3 0 0<br>(0)(6)(0)(0)                                                                                                                                                         | 3 1 0 0<br>(6)(2)(0)(0)                          | 3 4 0 0<br>(6)(8)(0)(0)                               | 5 8 0 0<br>(10) (16) (0) (0)                          |
|             | granulopoiesis:increased | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                  | 1 0 0 0<br>(2)(0)(0)(0)                          | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |
|             | hyperplasia:vascular     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 1 0 0 0<br>(2)(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

(c) c:b/a\*100

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

PAGE: 6

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|           |                              |                                                                        |                                        |                                        | PAGE :                                  |
|-----------|------------------------------|------------------------------------------------------------------------|----------------------------------------|----------------------------------------|-----------------------------------------|
|           |                              | Group Name 0 ppm<br>No. of Animals on Study 50<br>Grade <u>1 2 3 4</u> | 3 ppm<br>50<br><u>1 2 3 4</u>          | 10 ppm<br>50<br>_1 2 3 4               | 30 ppm<br>50<br>1 2 3 4                 |
| rgan      | _ Findings                   | (%) (%) (%)                                                            | (%) (%) (%) (%)                        | (%) (%) (%) (%)                        | (%) (%) (%) (%)                         |
| Hematopoi | etic system)                 |                                                                        |                                        |                                        |                                         |
| pleen     | deposit of hemosiderin       | <50><br>17 1 0 0<br>(34) (2) (0) (0)                                   | <50><br>4 0 0 0 ***<br>(8)(0)(0)(0)    | <50><br>2 0 0 0 **<br>(4)(0)(0)(0)     | <50><br>9 1 0 0<br>(18) (2) (0) (0)     |
|           | fibrosis                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                         | 5 0 0 0<br>(10) (0) (0) (0)            | 3 0 0 0<br>(6)(0)(0)(0)                | 10 0 1 0 ***<br>(20) (0) (2) (0)        |
|           | extramedullary hematopoiesis | 18 3 1 0<br>(36) (6) (2) (0)                                           | 29 2 3 0<br>(58) (4) (6) (0)           | 23 7 3 0<br>(46)(14)(6)(0)             | 19 9 6 0 <b>*</b><br>(38) (18) (12) (0) |
|           | follicular hyperplasia       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 1 0 0 0<br>(2)(0)(0)(0)                 |
| Circulato | ry system}                   |                                                                        |                                        |                                        |                                         |
| eart      | thrombus                     | <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>0 3 0 0<br>( 0) ( 6) ( 0) ( 0)  |
|           | inflammation                 | 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 2 0 0<br>( 0) ( 4) ( 0) ( 0)          |
|           | myocardial fibrosis          | 18 28 0 0<br>(36)(56)(0)(0)                                            | 34 15 0 0 **<br>(68) (30) (0) (0)      | 29 16 0 0<br>(58) (32) (0) (0)         | 35 9 0 0 **<br>(70) (18) (0) (0)        |

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- (c) c:b/a\*100

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

STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

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

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| Drgan         | Findings                  | Group Name<br>No. of Animals on Study<br>Grade <u>1</u> (%) | 0 ppm<br>50<br><u>2 3 4</u><br>(%) (%) (%) | 3 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|---------------|---------------------------|-------------------------------------------------------------|--------------------------------------------|--------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| Circulatory s | system)                   |                                                             |                                            |                                                  |                                                   | ъ,                                                |
| rtery/aort    | mineralization            | 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>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)            |
|               | arteritis                 | 0<br>( 0)                                                   | 1 0 0<br>(2)(0)(0)                         | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
| ein           | thrombus                  | 0<br>( 0)                                                   | <50><br>1 0 0<br>( 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)            |
| Digestive sys | stem)                     |                                                             |                                            |                                                  |                                                   |                                                   |
| ongue         | inflammatory infiltration | 1<br>( 2)                                                   | <50><br>0 0 0<br>( 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)            |
|               | arteritis                 | 1<br>( 2)                                                   | 0 0 0<br>( 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)                    |
| alivary gl    | atrophy                   | 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>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |

(c) c:b/a\*100

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

(HPT150)

PAGE : 8

| ANIMAL :<br>REPORT TYPE : |                           | HISTOLOGICAL FINDINGS :NON-NE<br>ALL ANIMALS (0-105W)                                                                                                                           | EOPLASTIC LESIONS (SUMMARY)                      |                                                   |                                                   |
|---------------------------|---------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| SEX :                     | MALE                      |                                                                                                                                                                                 |                                                  |                                                   | PAGE :                                            |
| Organ                     | Findings                  | Group Name         0 ppm           No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%) | 3 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| {Digestive sy             |                           |                                                                                                                                                                                 |                                                  |                                                   |                                                   |
| salivary gl               | abscess                   | <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)            |
| stomach                   | mineralization            | <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 1 0 0<br>( 0) ( 2) ( 0) ( 0)            | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
|                           | erosion:forestomach       | 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)                           |
|                           | ulcer:forestomach         | 0 2 1 0<br>( 0) ( 4) ( 2) ( 0)                                                                                                                                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 0 2 1 0<br>( 0) ( 4) ( 2) ( 0)                    | 1 1 1 0<br>(2)(2)(2)(0)                           |
|                           | hyperplasia forestomach   | 0 2 1 0<br>( 0) ( 4) ( 2) ( 0)                                                                                                                                                  | 0 2 0 0<br>( 0) ( 4) ( 0) ( 0)                   | 2 1 2 0<br>(4)(2)(4)(0)                           | 1 3 0 0<br>(2)(6)(0)(0)                           |
|                           | erosion:glandular stomach | 4 0 0 0<br>(8)(0)(0)(0)                                                                                                                                                         | 1 1 0 0<br>(2)(2)(0)(0)                          | 5 1 0 0<br>(10) (2) (0) (0)                       | 6 1 0 0<br>(12)(2)(0)(0)                          |
|                           | ulcer:glandular stomach   | 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)                    |
| liver                     | herniation                | <50><br>5 0 0 0<br>(10) (0) (0) (0)                                                                                                                                             | <50><br>10 0 0 0<br>(20) (0) (0) (0)             | <50><br>6 0 0 0<br>(12) (0) (0) (0)               | <50><br>3 0 0 0<br>(6) (0) (0) (0)                |

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

< a >

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

(c)

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

# (HPT150)

# BAIS3

| SEX       | : MALE                       |                                                           |                                                                                                                |                                                       | PAGE                                              |
|-----------|------------------------------|-----------------------------------------------------------|----------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|---------------------------------------------------|
| Organ     | Findings                     | Group Name0 ppmNo. of Animals on Study50Grade123(%)(%)(%) | $\begin{array}{c} 3 \text{ ppm} \\ 50 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | 30 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| Digestive | system)                      |                                                           |                                                                                                                |                                                       |                                                   |
| liver     | peliosis-like lesion         | <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>1 0 0 0<br>(2) (0) (0) (0)                |
|           | necrosis:central             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                            | 1 0 0 0<br>(2)(0)(0)(0)                                                                                        | 1 1 0 0<br>(2)(2)(0)(0)                               | 4 1 0 0<br>(8)(2)(0)(0)                           |
|           | necrosis:focal               | 2 1 0 0<br>(4)(2)(0)(0)                                   | 2 0 0 0<br>(4)(0)(0)(0)                                                                                        | 2 2 0 0<br>(4)(4)(0)(0)                               | 2 0 0 0<br>(4)(0)(0)(0)                           |
|           | fatty change                 | 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)                               | 2 0 0 0<br>(4)(0)(0)(0)                           |
|           | lymphocytic infiltration     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                 | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 1 0 0 0<br>(2)(0)(0)(0)                           |
|           | granulation                  | 13 1 0 0<br>(26)(2)(0)(0)                                 | 15 0 0 0<br>(30)(0)(0)(0)                                                                                      | 16 0 0 0<br>(32)(0)(0)(0)                             | 11 0 0 0<br>(22)(0)(0)(0)                         |
|           | perivascular inflammation    | 0 1 0 0<br>( 0) ( 2) ( 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                     |
|           | extramedullary hematopoiesis | 1 0 0 0<br>(2)(0)(0)(0)                                   | 3 0 0 0<br>(6)(0)(0)(0)                                                                                        | 1 0 0 0<br>(2)(0)(0)(0)                               | 4 0 0 0<br>(8)(0)(0)(0)                           |

くぉゝ b a : Number of animals examined at the site

b : Number of animals with lesion

c:b/a\*100 (c)

STUDY NO. : 0342 : RAT F344/DuCrj ANIMAL REPORT TYPE : A1 SEX : MALE

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

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| )rgan       | Findings               |                  | ·                       | 3 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|-------------|------------------------|------------------|-------------------------|--------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| Digestive : | system)                |                  |                         |                                                  |                                                   |                                                   |
| iver        | clear cell focus       | 4 0              | 50><br>0 0<br>( 0) ( 0) | <50><br>3 1 0 0<br>( 6) ( 2) ( 0) ( 0)           | <50><br>10 0 0 0<br>(20) (0) (0) (0)              | <50><br>3 0 0 0<br>( 6) ( 0) ( 0) ( 0)            |
|             | acidophilic cell focus | 6 1<br>(12) (2)  | 0 0<br>( 0) ( 0)        | 16 1 0 0<br>(32) (2) (0) (0)                     | 4 1 0 0<br>(8)(2)(0)(0)                           | 5 0 0 0<br>(10) (0) (0) (0)                       |
|             | basophilic cell focus  | 3 1<br>( 6) ( 2) | 0 0<br>( 0) ( 0)        | 21 0 0 0 **<br>(42) (0) (0) (0)                  | 16 2 0 0 **<br>(32) (4) (0) (0)                   | 3 1 0 0<br>(6)(2)(0)(0)                           |
|             | spongiosis hepatis     | 5 0<br>(10) (0)  | 0 0<br>( 0) ( 0)        | 3 1 0 0<br>(6)(2)(0)(0)                          | 3 1 0 0<br>(6)(2)(0)(0)                           | 6 0 0 0<br>(12)(0)(0)(0)                          |
|             | bile duct hyperplasia  | 48 2<br>(96) (4) | 0 0<br>( 0) ( 0)        | 49 1 0 0<br>(98) (2) (0) (0)                     | 47 3 0 0<br>(94)(6)(0)(0)                         | 44 6 0 0<br>(88)(12)(0)(0)                        |
|             | cholangiofibrosis      | 0 0<br>( 0) ( 0) | 0 0<br>( 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)                    |
|             | biliary cyst           | 1 0<br>(2)(0)    | 0 0<br>( 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)                    |
| ncreas      | atrophy                | 3 0              | 50><br>0 0<br>( 0) ( 0) | <49><br>3 0 0 0<br>( 6) ( 0) ( 0) ( 0)           | <50><br>2 0 0 0<br>(4)(0)(0)(0)                   | <50><br>4 0 0 0<br>(8)(0)(0)(0)                   |

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

b b : Number of animals with lesion

(c) c:b/a\*100

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

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PAGE : 11

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| SEX         | : MALE                 |                                                                                           |                                                  |                                                   | PAGE : 1                                          |
|-------------|------------------------|-------------------------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| Organ       | . Findings             | Group Name 0 ppm<br>No. of Animals on Study 50<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | 3 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| {Digestive  | system)                |                                                                                           |                                                  |                                                   |                                                   |
| pancreas    | islet cell hyperplasia | <50><br>3 2 0 0<br>(6)(4)(0)(0)                                                           | <49><br>2 1 0 0<br>( 4) ( 2) ( 0) ( 0)           | <50><br>2 1 0 0<br>( 4) ( 2) ( 0) ( 0)            | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)            |
| {Urinary sy | vstem)                 |                                                                                           |                                                  |                                                   |                                                   |
| kidney      | infarct                | <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)            |
|             | 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 1 0<br>( 0) ( 0) ( 2) ( 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)                    | 1 0 0 0<br>(2)(0)(0)(0)                           |
|             | eosinophilic body      | 46 0 0 0<br>(92) (0) (0) (0)                                                              | 45 0 0 0<br>(90)(0)(0)(0)                        | 46 2 0 0<br>(92) (4) (0) (0)                      | 45 0 0 0<br>(90)(0)(0)(0)                         |
|             | chronic nephropathy    | 13 23 13 0<br>(26) (46) (26) (0)                                                          | 10 19 18 0<br>(20) (38) (36) (0)                 | 8 23 18 0<br>(16)(46)(36)(0)                      | 9 18 20 0<br>(18) (36) (40) (0)                   |
|             | hydronephrosis         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 1 0 0 0<br>(2)(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

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

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| Drgan         | 1                                      | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | 0 ppm<br>50<br><u>2 3</u><br>(%) (%) | <u>4</u> <u>1</u><br>(%) (% | 2           |             | <u>4                                    </u> |     | 10<br>50<br>2<br>(%) | ppm<br><u>3</u><br>(%) | <u>4</u><br>(%) | -( | <u>1</u> (%) | 30<br>50<br><u>2</u><br>(%) | 0 ppm<br>0<br><u>3</u><br>(%) | 4        |
|---------------|----------------------------------------|----------------------------------------------------------------|--------------------------------------|-----------------------------|-------------|-------------|----------------------------------------------|-----|----------------------|------------------------|-----------------|----|--------------|-----------------------------|-------------------------------|----------|
|               |                                        |                                                                |                                      | ·                           |             |             |                                              |     |                      |                        |                 |    |              |                             |                               |          |
| {Urinary syst | em)                                    |                                                                |                                      |                             |             |             |                                              |     |                      |                        |                 |    |              |                             |                               |          |
| kidney        | mineralization:cortico-medullary junct |                                                                | <50><br>0 0<br>( 0) ( 0)             | 0 0<br>( 0) ( 0             |             |             | 0 1<br>0) (2)                                |     | <50><br>0<br>0) (    | 0                      | 0<br>0)         |    | 0<br>0) (    | <50<br>0<br>0)              | 0><br>0<br>( 0)               | 0<br>( 0 |
|               | mineralization:papilla                 | 0                                                              | 0 0<br>( 0) ( 0)                     | 0 1<br>(0) (2               | 0<br>) ( 0) | 0<br>( 0) ( | 0 0<br>0) ( 0)                               | ) ( | 0<br>0) (            | 0<br>0) (              | 0<br>0)         |    | 0<br>0) (    | 0<br>0)                     | 0<br>( 0)                     | ( (      |
|               | mineralization:pelvis                  | 0<br>( 0)                                                      | 0 0<br>( 0) ( 0)                     | 0 1<br>(0) (2               | 0<br>) ( 0) | 0<br>( 0) ( | 0 0<br>0) ( 0)                               | ) ( | 0<br>0) (            | 0<br>0) (              | 0<br>0)         | (  | 2<br>4) (    | 0<br>0)                     | 0<br>( 0)                     | ( (      |
|               | mineralization:cortex                  | 0<br>( 0)                                                      | 0 0<br>(0)(0)                        | 0 2<br>(0) (4               | 0<br>) ( 0) | 0<br>( 0) ( | 0 0<br>0) ( 0)                               | ) ( | 0<br>0) (            | 0<br>0) (              | 0<br>( 0)       | (  | 1<br>2) (    | 0<br>0)                     | 0<br>( 0)                     | ( (      |
| ırin bladd    | simple hyperplasia:transitional epithe |                                                                | <50><br>0 0<br>( 0) ( 0)             | 0 0<br>( 0) ( 0             |             |             | 0 0<br>0) ( 0)                               |     | <50><br>0<br>0) (    | 0                      | 0<br>( 0)       |    | 0<br>0) (    | <5<br>1<br>2)               | 0><br>0<br>( 0)               | (        |
|               | xanthogranuloma                        | 0<br>( 0)                                                      | 0 0<br>(0)(0)                        | 0 0<br>( 0) ( 0             |             | 0<br>( 0) ( | 0 1<br>0) (2)                                | ) ( | 0<br>0) (            | 0<br>0) (              | 0<br>( 0)       |    | 0<br>0) (    | 0<br>0)                     | 0<br>( 0)                     | (        |
| {Endocrine sy | stem}                                  |                                                                |                                      |                             |             |             |                                              |     |                      |                        |                 |    |              |                             |                               |          |
| pituitary     | angiectasis                            | 0<br>( 0)                                                      | <50><br>0 0<br>( 0) ( 0)             | 0 2<br>( 0) ( 4             |             |             | 0 1<br>0) ( 2)                               |     | <50><br>0<br>0) (    | 0                      | 0<br>( 0)       |    | 3<br>6) (    | 0                           | 0><br>0<br>( 0)               | ( (      |

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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| Organ        | Findings                          | Group Name         0 ppm           No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%) | $\begin{array}{c} 3 \text{ ppm} \\ 50 \\ \hline 1 & 2 & 3 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | 10 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
|--------------|-----------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------|---------------------------------------------------|-------------------------------------------------------|
| {Endocrine s | ystem)                            |                                                                                                                                                                                 |                                                                                                            |                                                   |                                                       |
| pituitary    | 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>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)            | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
|              | cyst                              | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                                                                           | 2 0 0 0<br>(4)(0)(0)(0)                                                                                    | 2 0 0 0<br>(4)(0)(0)(0)                           | 3 0 0 0<br>(6)(0)(0)(0)                               |
|              | hyperplasia                       | 11 2 0 0<br>(22) (4) (0) (0)                                                                                                                                                    | 7 2 0 0<br>(14) (4) (0) (0)                                                                                | 6 5 0 0<br>(12)(10)(0)(0)                         | 1 1 0 0 **<br>(2)(2)(0)(0)                            |
|              | Rathke pouch                      | 5 0 0 0<br>(10) (0) (0) (0)                                                                                                                                                     | 1 0 0 0<br>(2)(0)(0)(0)                                                                                    | 1 0 0 0<br>(2)(0)(0)(0)                           | 2 1 0 0<br>( 4) ( 2) ( 0) ( 0)                        |
|              | focal hypertrophy                 | 4 0 0 0<br>(8)(0)(0)(0)                                                                                                                                                         | 8 1 0 0<br>(16)(2)(0)(0)                                                                                   | 4 0 0 0<br>(8)(0)(0)(0)                           | 3 1 0 0<br>(6)(2)(0)(0)                               |
| hyroid       | ultimibranchial body remanet      | <50><br>1 0 0 0<br>( 2) ( 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)            | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                |
|              | C-cell hyperplasia                | 11 0 0 0<br>(22) (0) (0) (0)                                                                                                                                                    | 10 1 0 0<br>(20) (2) (0) (0)                                                                               | 7 1 1 0<br>(14) (2) (2) (0)                       | 4 0 0 0<br>(8)(0)(0)(0)                               |
|              | focal follicular cell hyperplasia | 4 0 0 0<br>(8)(0)(0)(0)                                                                                                                                                         | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                                                                             | 3 0 0 0<br>(6)(0)(0)(0)                           | 3 2 0 0<br>(6)(4)(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

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

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| Drgan       | Findings                     | Group Name         0 ppm           No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $\begin{array}{c} 3 \text{ ppm} \\ 50 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | 10 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|-------------|------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| Endocrine s | system)                      |                                                                                                                                                                                             |                                                                                                                |                                                   |                                                   |
| drenal      | extramedullary hematopoiesis | <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)            | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)            |
|             | hyperplasia:cortical cell    | 4 0 0 0<br>( 8) ( 0) ( 0) ( 0)                                                                                                                                                              | 3 0 0 0<br>(6)(0)(0)(0)                                                                                        | 4 1 0 0<br>(8)(2)(0)(0)                           | 5 1 0 0<br>(10) (2) (0) (0)                       |
|             | hyperplasia:medulla          | 6 0 0 0<br>(12)(0)(0)(0)                                                                                                                                                                    | 5 0 0 0<br>(10) (0) (0) (0)                                                                                    | 2 2 0 0<br>(4)(4)(0)(0)                           | 5 0 0 0<br>(10) (0) (0) (0)                       |
|             | focal fatty change:cortex    | 9 1 1 0<br>(18) (2) (2) (0)                                                                                                                                                                 | 12 1 0 0<br>(24) (2) (0) (0)                                                                                   | 7 0 0 0<br>(14) ( 0) ( 0) ( 0)                    | 10 1 0 0<br>(20) (2) (0) (0)                      |
| leproductiv | 7e system)                   |                                                                                                                                                                                             |                                                                                                                |                                                   |                                                   |
| estis       | atrophy                      | <50><br>1 2 40 0<br>( 2) ( 4) ( 80) ( 0)                                                                                                                                                    | <50><br>3 9 33 0<br>( 6) ( 18) ( 66) ( 0)                                                                      | <50><br>1 7 40 0<br>( 2) ( 14) ( 80) ( 0)         | <50><br>1 2 46 0<br>( 2) ( 4) ( 92) ( 0)          |
|             | mineralization               | 5 0 0 0<br>(10) (0) (0) (0)                                                                                                                                                                 | 4 1 0 0<br>(8)(2)(0)(0)                                                                                        | 7 0 0 0<br>(14) (0) (0) (0)                       | 2 0 0 0<br>(4)(0)(0)(0)                           |
|             | arteritis                    | 2 1 0 0<br>( 4) ( 2) ( 0) ( 0)                                                                                                                                                              | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                                                                                 | 0 2 0 0<br>( 0) ( 4) ( 0) ( 0)                    | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                    |

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

| REPORT TYPE : | RAT F344/DuCrj<br>A1<br>MALE  | ALL ANIMALS (0-105W)                                                                                                                                                                        |                                                  |                                                   | PAGE : 1                                              |
|---------------|-------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------|-------------------------------------------------------|
| Organ         | Findings                      | Group Name         0 ppm           No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | 3 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
| {Reproductive | system}                       |                                                                                                                                                                                             |                                                  |                                                   |                                                       |
| testis        | interstitial cell hyperplasia | <50><br>5 1 0 0<br>(10) (2) (0) (0)                                                                                                                                                         | <50><br>4 0 0 0<br>( 8) ( 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)                    |
| semin ves     | inflammation                  | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                      | <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)                |
| prostate      | inflammation                  | <50><br>9 7 1 0<br>(18) (14) (2) (0)                                                                                                                                                        | <50><br>8 8 1 0<br>(16) (16) (2) (0)             | <50><br>8 5 1 0<br>(16) (10) (2) (0)              | <50><br>9 3 1 0<br>(18) (6) (2) (0)                   |
|               | hyperplasia                   | 12 0 0 0<br>(24) (0) (0) (0)                                                                                                                                                                | 6 1 0 0<br>(12)(2)(0)(0)                         | 15 0 0 0<br>(30)(0)(0)(0)                         | 12 0 0 0<br>(24) (0) (0) (0)                          |
| mammary gl    | duct ectasia                  | <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)                |
|               | hyperplasia                   | 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)                        |
|               | galactocele                   | 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)                           | 4 0 0 0<br>(8)(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  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

BAIS3

: RAT F344/DuCrj ANIMAL ALL ANIMALS (0-105W) REPORT TYPE : A1 : MALE SEX PAGE: 17 Group Name 0 ppm 3 ppm 10 ppm 30 ppm No. of Animals on Study 50 50 50 50 Grade 2 3 4 3 4 2 3 2 3 4 4 Organ\_\_\_\_ Findings\_ (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) {Nervous system} brain <50> <50> <50> <50> hemorrhage 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 (0) (0) (0) (0)( 0) ( 0) ( 0) ( 0) (2) (0) (0) (0) (0) (0) (0) (0)necrosis:focal 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 (0) (0) (0) (0)(0) (0) (0) (0)(0) (0) (0) (0)(0)(2)(0)(0) gliosis 0 1 0 0 0 0 0 0 0 0 0 2 1 0 0 0 (0) (2) (0) (0) (0) (0) (0) (0)(0) (2) (0) (0) (4)(0)(0)(0) vacuolic change:nerve cell 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 ( 0) ( 0) ( 0) ( 0) (0) (0) (0) (0)(2) (0) (0) (0)(0)(0)(0)(0) spinal cord <50> <50> <50> <50> gliosis 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 (0) (0) (0) (0)(0) (0) (0) (0)(0) (2) (0) (0) (0)(0)(0)(0) {Special sense organs/appendage} eye <50> <50> <50> <50> hemorrhage 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 (2) (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 : 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

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HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

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(HPT150)

STUDY NO. : 0342

BAIS3

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

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| rgan        | Findings                 | Group Name         0 ppm           No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $\begin{array}{c} 3 \text{ ppm} \\ 50 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | 10 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|-------------|--------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| Special sen | se organs/appendage}     |                                                                                                                                                                                             |                                                                                                                |                                                   |                                                   |
| уe          | cataract                 | <50><br>1 1 3 0<br>( 2) ( 2) ( 6) ( 0)                                                                                                                                                      | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                         | <50><br>1 0 1 0<br>( 2) ( 0) ( 2) ( 0)            | <50><br>0 3 0 0<br>( 0) ( 6) ( 0) ( 0)            |
|             | retinal atrophy          | 45 0 2 0<br>(90) (0) (4) (0)                                                                                                                                                                | 46 0 0 0<br>(92)(0)(0)(0)                                                                                      | 40 0 1 0<br>(80) (0) (2) (0)                      | 34 0 2 0 *<br>(68) ( 0) ( 4) ( 0)                 |
|             | keratitis                | 1 0 0 0<br>(2)(0)(0)(0)(0)                                                                                                                                                                  | 0 0 1 0<br>(0)(0)(2)(0)                                                                                        | 0 0 0 0<br>(0)(0)(0)(0)                           | 3 1 2 0<br>(6)(2)(4)(0)                           |
|             | iritis                   | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                            | 0 0 0 0<br>(0)(0)(0)(0)(0)                                                                                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                    |
| rder gl     | degeneration             | <50><br>3 2 0 0<br>( 6) ( 4) ( 0) ( 0)                                                                                                                                                      | <50><br>4 1 0 0<br>( 8) ( 2) ( 0) ( 0)                                                                         | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0)            | _<50><br>5 1 0 0<br>(10) (2) (0) (0)              |
|             | lymphocytic infiltration | 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)                           | 1 0 0 0<br>(2)(0)(0)(0)                           |
| mbal gl     | inflammation             | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                      | <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)            |

b : Number of animals with lesion ь (c)

c:b/a\*100

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

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| Organ                   | Findings                                                                                                        | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%)     | 0 ppm<br>50<br>(%) (%) (%)    | 3 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|-------------------------|-----------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------|-------------------------------|--------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| {Musculoskel            | etal system)                                                                                                    |                                                                    |                               |                                                  |                                                   |                                                   |
| nuscle                  | atrophy                                                                                                         | 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>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <50><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)            |
| Body caviti             | es)                                                                                                             |                                                                    |                               |                                                  |                                                   |                                                   |
| ₽ritoneum               | cyst                                                                                                            | 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>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
|                         | peritonitis                                                                                                     | 0<br>( 0) (                                                        | 1 0 0<br>2) ( 0) ( 0)         | 0 0 0 0 0                                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|                         | mesothelial hyperplasia                                                                                         | 0<br>( 0) (                                                        | 0 0 0<br>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)                           |
| rade<br>a ><br>b<br>c ) | 1: Slight 2: Moderate<br>a: Number of animals examined at<br>b: Number of animals with lesion<br>c: b / a * 100 | 3 : Marked 4 : Severe<br>the site<br>: P ≤ 0.01 Test of Chi Square |                               |                                                  |                                                   |                                                   |

(HPT150)

BAIS3

APPENDIX J 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

| STUDY NO.   | : | 0342           |
|-------------|---|----------------|
| ANIMAL      | : | RAT F344/DuCrj |
| REPORT TYPE | : | A1             |
| SEX         | : | MALE           |

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**`**\_\_\_\_

| )rgan         |                                        | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | 0 ppm<br>10<br><u>2 3 4</u><br>(%) (%) (%) | 3 ppm<br>8<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>12<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>27<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|---------------|----------------------------------------|----------------------------------------------------------------|--------------------------------------------|-------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| (Integumentar | y system/appandage}                    |                                                                |                                            |                                                 |                                                   |                                                   |
| skin/app      | inflammation                           | 0<br>( 0)                                                      | <10><br>0 0 0<br>( 0) ( 0) ( 0)            | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)          | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <27><br>0 1 0 0<br>( 0) ( 4) ( 0) ( 0)            |
|               | hyperplasia:epidermis                  | 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>(4)(0)(0)(0)                           |
| {Respiratory  | system)                                |                                                                |                                            |                                                 |                                                   |                                                   |
| asal cavit    | thrombus                               | . 0 ( 0)                                                       | <10><br>2 2 0<br>( 20) ( 20) ( 0)          | < 8><br>1 0 2 0<br>(13) (0) (25) (0)            | <12><br>2 1 1 0<br>( 17) ( 8) ( 8) ( 0)           | <277><br>1 1 0 0 *<br>( 4) ( 4) ( 0) ( 0)         |
|               | mineralization                         | 9<br>(90)                                                      | 0 0 0<br>( 0) ( 0) ( 0)                    | 6 0 0 0<br>(75)(0)(0)(0)                        | 8 0 0 0<br>(67)(0)(0)(0)                          | 23 0 0 0<br>(85)(0)(0)(0)                         |
|               | eosinophilic change:olfactory epitheli |                                                                | 0 0 0<br>( 0) ( 0) ( 0)                    | 5 0 0 0<br>(63)(0)(0)(0)                        | 3 0 1 0<br>(25)(0)(8)(0)                          | 17 0 0 0<br>(63)(0)(0)(0)                         |
|               | eosinophilic change!respiratory epithe |                                                                | 0 0 0<br>( 0) ( 0) ( 0)                    | 3 0 0 0<br>(38)(0)(0)(0)                        | 5 0 0 0<br>(42)(0)(0)(0)                          | 6 1 0 0<br>(22) (4) (0) (0)                       |
|               | inflammation:foreign body              | 1<br>(10)                                                      | 0 0 0<br>( 0) ( 0) ( 0)                    | 2 3 0 0*<br>(25)(38)(0)(0)                      | 5 0 0 0<br>(42)(0)(0)(0)                          | 10 0 0 0<br>(37) (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

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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| )rgan       | Group Name<br>No. of Animals of<br>Grade                      | n Study<br>(%) | (<br>1(<br>2<br>(%) | ) ppm<br>)<br><u>3</u><br>(%) | 4 (%)     | <u> </u>   | 3<br>8<br><u>2</u><br>(%) | ppm<br><u>3 4</u><br>(%) (%) | <u> </u>    | 10<br>12<br>2<br>(%) | ppm<br><u>3</u><br>(%) | 4 (%)     | <u> </u>    | 31<br>2'<br><u>2</u><br>(%) | 0 ppm<br>7<br><u>3</u><br>(%) | 4(%)        |
|-------------|---------------------------------------------------------------|----------------|---------------------|-------------------------------|-----------|------------|---------------------------|------------------------------|-------------|----------------------|------------------------|-----------|-------------|-----------------------------|-------------------------------|-------------|
| Respiratory | system)                                                       |                |                     |                               |           |            |                           |                              |             |                      |                        |           |             |                             |                               |             |
| asal cavit  | inflammation:respiratory epithelium                           | 1<br>(10)      | <1(<br>0<br>( 0)    | 0                             | 0<br>( 0) | 1<br>(13)  | < 8<br>0<br>( 0) (        | ><br>0 0<br>0) ( 0)          | 0<br>( 0)   | <12<br>0<br>( 0) (   | 0                      | 0<br>( 0) | 4<br>(15)   | <2"<br>12<br>( 44)          | 7><br>0<br>( 0) (             | 0*<br>(0)   |
|             | respiratory metaplasia:olfactory epithelium                   | 1<br>(10)      | 0<br>( 0)           | 0<br>( 0)                     | 0<br>( 0) | 0<br>( 0)  | 0<br>( 0) (               | 0 0<br>0) ( 0)               | 1<br>( 8)   | 0<br>( 0) (          | 0<br>0)                | 0<br>( 0) | 2<br>( 7)   | 0<br>( 0)                   | 0<br>( 0) (                   | 0<br>( 0)   |
|             | respiratory metaplasia:gland                                  | 6<br>(60)      | 0<br>( 0)           | 0<br>( 0)                     | 0<br>( 0) | 7<br>( 88) | 0<br>( 0) (               | 0 0<br>0) ( 0)               | 11<br>( 92) | 0<br>( 0) (          | 0<br>0)                | 0<br>( 0) | 22<br>( 81) | 0<br>( 0)                   | 0                             | 0<br>( 0)   |
|             | inflammation:transitional epithelium                          | 1<br>(10)      | 0<br>( 0)           | 0<br>( 0)                     | 0<br>( 0) | 0<br>( 0)  | 0<br>( 0) (               | 0 0<br>0) ( 0)               | 0<br>( 0)   | 0<br>( 0) (          | 0<br>0)                | 0<br>( 0) | 0<br>( 0)   | 0<br>( 0)                   | 0<br>( 0) (                   | 0<br>( 0)   |
|             | squamous cell metaplasia:respiratory epithelium               | 1<br>(10)      | 0<br>( 0)           | 0<br>( 0)                     | 0<br>( 0) | 1<br>(13)  | 0<br>( 0) (               | 0 0<br>0) ( 0)               | 1<br>( 8)   | 0<br>( 0) (          | 0<br>0)                | 0<br>( 0) | 1<br>( 4)   | 0<br>( 0)                   | 1<br>( 4) (                   | 0<br>( 0)   |
|             | squamous cell metaplasia with atypia:respiratory epith<br>ium | el 0<br>(0)    | 0<br>( 0)           | 0<br>( 0)                     | 0<br>( 0) | 0<br>( 0)  | 0<br>( 0) (               | 0 0<br>0) ( 0)               | 4<br>(33)   | 0<br>( 0) (          | 0<br>0)                | 0<br>( 0) | 4<br>(15)   | 21<br>(78)                  | 0                             | ( 0)        |
|             | squamous cell hyperplasia with atypia                         | 0<br>( 0)      | 0<br>( 0)           | 0<br>( 0)                     | 0<br>( 0) | 0<br>( 0)  | 0<br>( 0) (               | 0 0<br>0) ( 0)               | 0<br>( 0)   | 0<br>( 0) (          | 0<br>0)                | 0<br>( 0) | 10<br>(37)  | 9<br>(33)                   | 0                             | 0 ×<br>( 0) |
|             | hyperplasia with atypia:respiratory epithelium                | 0<br>( 0)      | 0<br>( 0)           | 0<br>( 0)                     | 0<br>( 0) | 0<br>( 0)  | 0<br>( 0) (               | 0 0<br>0) ( 0)               | 0<br>( 0)   | 0<br>( 0) (          | 0<br>0)                | 0<br>( 0) | 3<br>(11)   | 0<br>( 0)                   | 0                             | 0<br>( 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

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

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| •            |                                         |                                                             |                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                       |                                                   |
|--------------|-----------------------------------------|-------------------------------------------------------------|------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|---------------------------------------------------|
| Organ        | N                                       | roup Name<br>c. of Animals on Study<br>rade <u>1</u><br>(%) | 0 ppm<br>10<br><u>2 3</u><br>) (%) (%) ( | $ \frac{4}{(\%)} \frac{1}{(\%)} \frac{2}{(\%)} \frac{3}{(\%)} \frac{9}{(\%)} \frac{3}{(\%)} \frac{9}{(\%)} \frac{3}{(\%)} \frac{9}{(\%)} \frac{3}{(\%)} \frac{3}{(\%)} \frac{9}{(\%)} 9$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | 30 ppm<br>27<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| {Respiratory | system)                                 |                                                             |                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                       |                                                   |
| nasal cavit  | hyperplasia with atypia:nasal gland     | 0<br>( 0)                                                   | <10><br>0 0<br>0 ( 0) ( 0) (             | < 8><br>0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <27><br>0 1 0 0<br>( 0) ( 4) ( 0) ( 0)            |
|              | hyperplasia with atypia:transitional ep |                                                             | 0 0<br>( 0) ( 0) (                       | 0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 1 0 0 0<br>(8)(0)(0)(0)                               | 3 0 0 0<br>(11)(0)(0)(0)                          |
|              | hyperplasia:transitional epithelium     | 0<br>( 0)                                                   | 0 0<br>( 0) ( 0) (                       | 0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 1 1 0 0<br>( 4) ( 4) ( 0) ( 0)                    |
|              | atrophy:olfactory epithelium            | 0<br>( 0)                                                   | 0 0<br>( 0) ( 0) (                       | 0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 7 0 0 0<br>(26)(0)(0)(0)                          |
|              | necrosis:olfactory epithelium           | 0<br>( 0)                                                   | 0 0<br>( 0) ( 0) (                       | 0 1 0 0 0<br>0) (13) (0) (0) (0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 3 0 0 0<br>(11)(0)(0)(0)                          |
|              | necrosis:respiratory epithelium         | 0<br>( 0)                                                   | 0 0<br>( 0) ( 0) (                       | 0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 1 0 0 0<br>(8)(0)(0)(0)                               | 3 2 1 0<br>(11) (7) (4) (0)                       |
|              | hyperplasia:respiratory epithelium      | 0<br>( 0)                                                   | 0 0<br>) ( 0) ( 0) (                     | 0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 3 0 0 0<br>(11)(0)(0)(0)                          |
|              | thickening of bone:turbinate            | 0<br>( 0)                                                   | 0 0<br>) ( 0) ( 0) (                     | 0 <sup>°</sup> 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 4 3 0 0*<br>(33)(25)(0)(0)                            | 8 4 0 0 *<br>(30)(15)(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.   | : | 0342           |
|-------------|---|----------------|
| ANIMAL      | ; | RAT F344/DuCrj |
| REPORT TYPE | : | A1             |
| SEX         | : | MALE           |

| Organ        | Findings                             | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | 0 ppm<br>10<br><u>2 3 4</u><br>(%) (%) (%) | 3 ppm<br>8<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>12<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>27<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|--------------|--------------------------------------|----------------------------------------------------------------|--------------------------------------------|-------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| {Respiratory | v system)                            |                                                                |                                            |                                                 |                                                   |                                                   |
| larynx       | inflammation                         | 1<br>(10)                                                      | <10><br>0 0 0<br>( 0) ( 0) ( 0)            | < 8><br>1 0 0 0<br>(13) (0) (0) (0)             | <12><br>1 0 0 0<br>( 8) ( 0) ( 0) ( 0)            | <27><br>3 0 0 0<br>( 11) ( 0) ( 0) ( 0)           |
| lung         | congestion                           | 0<br>( 0)                                                      | <10><br>1 0 0<br>( 10) ( 0) ( 0)           | < 8><br>0 2 0 0<br>( 0) ( 25) ( 0) ( 0)         | <12><br>1 1 0 0<br>( 8) ( 8) ( 0) ( 0)            | <27><br>0 2 0 0<br>( 0) ( 7) ( 0) ( 0)            |
|              | hemorrhage                           | 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 1 0 0<br>( 0) ( 4) ( 0) ( 0)                    |
|              | edema                                | 0<br>( 0)                                                      | 0 0 0<br>( 0) ( 0) ( 0)                    | 0 1 0 0<br>( 0) ( 13) ( 0) ( 0)                 | 1 1 0 0<br>(8)(8)(0)(0)                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|              | perivascular inflammation            | 0<br>( 0)                                                      | 0 0 0<br>( 0) ( 0) ( 0)                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                  | 0 1 0 0<br>( 0) ( 8) ( 0) ( 0)                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|              | accumulation of foamy cells          | 0<br>( 0)                                                      | 0 0 0<br>( 0) ( 0) ( 0)                    | 1 0 0 0<br>(13)(0)(0)(0)                        | 0 0 0 0<br>(0)(0)(0)(0)                           | 1 0 0 0<br>(4)(0)(0)(0)(0)                        |
|              | bronchiolar-alveolar cell hyperplasi |                                                                | 0 0 0<br>( 0) ( 0) ( 0)                    | 0 0 0 0<br>(0)(0)(0)(0)(0)                      | 0 1 0 0<br>( 0) ( 8) ( 0) ( 0)                    | 2 2 0 0<br>(7)(7)(0)(0)                           |
|              | inflammation:foreign body            | 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 1 0 0<br>( 0) ( 4) ( 0) ( 0)                    |

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

a : Number of animals examined at the site <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

| STUDY NO.   | : | 0342           |
|-------------|---|----------------|
| ANIMAL      | : | RAT F344/DuCrj |
| REPORT TYPE | : | A1             |
| SEX         | : | MALE           |

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rgan	Findings	Group Name         0 ppm           No. of Animals on Study         10           Grade         1         2         3           (%)         (%)         (%)         (%)	<u> </u>	pm <u>3 4</u> <u>1 2</u> <u>%</u> ) (%) (%	10 ppm 12 3 <u>3 4</u> ) (%) (%)	30 ppm 27 <u>1 2 3 4</u> (%) (%) (%) (%)
Respiratory	system)					
ung	hyperplasia:terminal bronchicle	<10> 0 0 0 ( 0) ( 0) ( 0)	<pre></pre>	0 0 0 0		<27> 1 0 0 0 ( 4) ( 0) ( 0) ( 0)
Hematopoieti	c system)					
one marrow	hemorrhage	(10) 0 0 0 ( 0) ( 0) ( 0)		0 0 0 0	<12> 0 0 0 0) ( 0) ( 0)	<27> 0 1 0 0 ( 0) ( 4) ( 0) ( 0)
	proliferation:histiocyte	0 0 1 ( 0) ( 0) ( 10)	0 0 0 ( 0) ( 0) ( 0) (	0 0 0 0 0)(0)(0)(0)		0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	increased hematopoiesis	0 0 0 ( 0) ( 0) ( 0)	0 0 0 ( 0) ( 0) ( 0) (	0 0 0 0 0)(0)(0)(0)		3 0 0 0 (11) ( 0) ( 0) ( 0)
	decreased hematopoiesis	0 0 0 ( 0) ( 0) ( 0)		0 0 0 0 0)(0)(0)(0)		1 0 0 0 (4)(0)(0)(0)
	erythropoiesis:increased	0 3 0 (0)(30)(0)		0 0 2 3 0)(0)(17)(25		2 8 0 0 (7)(30)(0)(0)
	granulopoiesis:increased	0 0 0 ( 0) ( 0) ( 0)		0 0 0 1 0) ( 0) ( 0) ( 8		0 0 0 0 ( 0) ( 0) ( 0) ( 0)

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

a : Number of animals examined at the site < 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

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

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Organ	Findings	Group Name         0 ppm           No. of Animals on Study         10           Grade         1         2         3         4           (%)         (%)         (%)         (%)	3 ppm 8 <u>1 2 3 4</u> (%) (%) (%) (%)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	30 ppm 27 <u>1 2 3 4</u> (%) (%) (%) (%)
(Hematopoieti	ic system)				
bone marrow	hyperplasia:vascular	<10> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<27> 1 0 0 0 ( 4) ( 0) ( 0) ( 0)
spleen	deposit of hemosiderin	<10> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 1 0 0 0 (13) (0) (0) (0)	<12> 2 0 0 0 ( 17) ( 0) ( 0) ( 0)	<27> 5 1 0 0 (19) (4) (0) (0)
	fibrosis	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (8)(0)(0)(0)	3 0 1 0 (11) (0) (4) (0)
	extramedullary hematopoiesis	0 2 1 0 ( 0) ( 20) ( 10) ( 0)	3 0 2 0 (38) (0) (25) (0)	1 3 3 0 (8)(25)(25)(0)	7 6 6 0 (26) (22) (22) (0)
	follicular 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 ( 4) ( 0) ( 0) ( 0)
{Circulatory	system)				
heart	thrombus	<10> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<27> 0 3 0 0 ( 0) ( 11) ( 0) ( 0)
Grade < a > b ( c ) Significant d	<pre>1 : Slight 2 : Moderate a : Number of animals examined at t b : Number of animals with lesion c : b / a * 100 difference ; * : P ≤ 0.05 **:</pre>	3 : Marked 4 : Severe he site P ≤ 0.01 Test of Chi Square			

(HPT150)

BAIS3

STUDY NO.	:	0342
ANIMAL	:	RAT F344/DuCrj
REPORT TYPE	:	A1
SEX	:	MALE .

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Organ		p Name 0 ppm of Animals on Study 10 e <u>1 2 3 4</u> (%) (%) (%) (%)	3 ppm 8 <u>1 2 3 4</u> (%) (%) (%) (%)	10 ppm 12 <u>1 2 3 4</u> (%) (%) (%) (%)	30 ppm 27 <u>1 2 3 4</u> (%) (%) (%) (%)
{Circulatory	system}				
heart	• inflammation	<10> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<27> 0 2 0 0 ( 0) ( 7) ( 0) ( 0)
	myocardial fibrosis	2 5 0 0 (20)(50)(0)(0)	6 2 0 0 * (75)(25)(0)(0)	7 3 0 0 (58)(25)(0)(0)	20 1 0 0 *** (74) ( 4) ( 0) ( 0)
artery/aort	mineralization	<10> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<27> 1 0 0 0 ( 4) ( 0) ( 0) ( 0)
	arteritis	0 1 0 0 ( 0) ( 10) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
vein	thrombus	$\begin{array}{c} <10 \\ 0 & 1 & 0 & 0 \\ ( & 0) & ( & 10) & ( & 0) \\ \end{array}$	<pre></pre>	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<27> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
{Digestive sy	stem)				
salivary gl	atrophy	<10> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 1 0 0 0 (13) (0) (0) (0)	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<27> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
Grade < a > b ( c )	1 : Slight 2 : Moderate 3 : Mu a : Number of animals examined at the site b : Number of animals with lesion c : b / a * 100	arked 4 : Severe			

(HPT150)

STUDY NO.	:	0342
ANIMAL	:	RAT F344/DuCrj
REPORT TYPE	:	A1
SEX	:	MALE

Organ	Findings	Group Name         0 ppm           No. of Animals on Study         10           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%)	3 ppm 8 <u>1 2 3 4</u> (%) (%) (%) (%)	10 ppm 12 <u>1 2 3 4</u> (%) (%) (%) (%)	30 ppm 27 <u>1 2 3 4</u> (%) (%) (%) (%)
{Digestive sys	stem)				
salivary gl	abscess	<10> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<12> 1 0 0 0 ( 8) ( 0) ( 0) ( 0)	<27> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
stomach	mineralization	<10> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<12> 0 1 0 0 ( 0) ( 8) ( 0) ( 0)	<27> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	erosion:forestomach	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (13) (0) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 ( 4) ( 0) ( 0) ( 0)
	ulcer:forestomach	0 2 1 0 ( 0) ( 20) ( 10) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 2 1 0 ( 0) ( 17) ( 8) ( 0)	1 0 1 0 (4)(0)(4)(0)
	hyperplasia:forestomach	0 2 1 0 ( 0) ( 20) ( 10) ( 0)	0 1 0 0 ( 0) ( 13) ( 0) ( 0)	1 1 2 0 (8) (8) (17) (0)	1 2 0 0 ( 4) ( 7) ( 0) ( 0)
	erosion:glandular stomach	1 0 0 0 (10) (0) (0) (0)	0 1 0 0 ( 0) ( 13) ( 0) ( 0)	2 1 0 0 (17) (8) (0) (0)	4     1     0     0       (15)     (4)     (0)     (0)
	ulcer:glandular stomach	0 0 0 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)
liver	herniation	<10> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 4 0 0 0 * ( 50) ( 0) ( 0) ( 0)	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<27> 3 0 0 0 ( 11) ( 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 : 8

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STUDY NO.	:	0342
ANIMAL	:	RAT F344/DuCrj
REPORT TYPE	:	A1
SEX	:	MALE

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Organ	_ Findings	Group Name         0 ppm           No. of Animals on Study         10           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%)	3 ppm 8 <u>1 2 3 4</u> (%) (%) (%) (%)	10 ppm 12 <u>1 2 3 4</u> (%) (%) (%) (%)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		
{Digestive	system)						
liver	necrosis:central	<10> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 1 0 0 0 (13) (0) (0) (0)	<12> 1 1 0 0 ( 8) ( 8) ( 0) ( 0)	<27> 3 1 0 0 (11) (4) (0) (0)		
	necrosis:focal	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 2 0 0 (17) (17) (0) (0)	2 0 0 0 (7)(0)(0)(0)		
	granulation	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 (4)(0)(0)(0)		
	extramedullary hematopoiesis	1 0 0 0 (10) (0) (0) (0)	1 0 0 0 (13) (0) (0) (0)	1 0 0 0 (8)(0)(0)(0)	3 0 0 0 (11) (0) (0) (0)		
	clear cell focus	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0	1 0 0 0 (4)(0)(0)(0)		
	acidophilic cell focus	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 0 0 0 (7)(0)(0)(0)		
	basophilic cell focus	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 0 0 0 (25)(0)(0)(0)	1 0 0 0 (8)(0)(0)(0)	1 1 0 0 (4)(4)(0)(0)		
	spongiosis hepatis	1 0 0 0 (10) (0) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 0 0 0 (7)(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.	:	0342
ANIMAL	:	RAT F344/DuCrj
REPORT TYPE	;	AI
SEX	:	MALE

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Organ	Ν	roup Name 0 ppm o. of Animals on Study 10 rade <u>1 2 3 4</u> (%) (%) (%) (%)	3 ppm 8 <u>1 2 3 4</u> (%) (%) (%) (%)	10 ppm 12 <u>1 2 3 4</u> (%) (%) (%) (%)	30 ppm 27 <u>1 2 3 4</u> (%) (%) (%) (%)
{Digestive s	system}				
iver	bile duct hyperplasia	<10> 10 0 0 0 (100) ( 0) ( 0) ( 0)	< 8> 8 0 0 0 (100) ( 0) ( 0) ( 0)	<12> 12 0 0 0 (100) ( 0) ( 0) ( 0)	<27> 24 3 0 0 (89) (11) (0) (0)
	cholangiofibrosis	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 (0)(0)(0)(0)	1 0 0 0 (8)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
ancreas	atrophy	$\begin{array}{cccc} <10 \\ 1 & 0 & 0 \\ (10) & (0) & (0) & (0) \end{array}$	< 8> 1 0 0 0 (13) (0) (0) (0)	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<27> 1 0 0 0 ( 4) ( 0) ( 0) ( 0)
	islet cell hyperplasia	2 0 0 0 (20) (0) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (8)(0)(0)(0)	1 0 0 0 (4)(0)(0)(0)
Urinary sy	stem)				
idney	infarct	<10> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<12> 1 0 0 0 ( 8) ( 0) ( 0) ( 0)	<27> 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 1 0 ( 0) ( 0) ( 4) ( 0)
rade a > b c )	<pre>1 : Slight 2 : Moderate 3 : a : Number of animals examined at the sit b : Number of animals with lesion c : b / a * 100 difference; * : P ≤ 0.05 ** : P ≤</pre>	Marked 4 : Severe e			

(HPT150)

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#### STUDY NO. : 0342 : RAT F344/DuCrj ANIMAL REPORT TYPE : A1 SEX : MALE

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

)rgan		up Name 0 ppm of Animals on Study 10 de <u>1 2 3 4</u> (%) (%) (%) (%)		$ \begin{array}{c} 10 \text{ ppm} \\ 12 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $	30 ppm 27 <u>1 2 3 4</u> (%) (%) (%) (%)
Urinary syst	em)				
idney	cyst	<10> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<27> 1 0 0 0 ( 4) ( 0) ( 0) ( 0)
	eosinophilic body	6 0 0 0 (60)(0)(0)(0)		9 2 0 0 (75)(17)(0)(0)	24 0 0 0 (89)(0)(0)(0)
	chronic nephropathy	4 3 2 0 (40) (30) (20) (0)	4 1 0 0 (50)(13)(0)(0)	1 8 2 0 (8)(67)(17)(0)	8 10 6 0 (30)(37)(22)(0)
	hydronephrosis	0 0 0 0 (0)(0)(0)(0)		0 0 0 0 (0)(0)(0)(0)(0)	1 0 0 0 (4)(0)(0)(0)
	mineralization:cortico-medullary junction	0 0 0 0 (0)(0)(0)(0)		1 0 0 0 (8)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	mineralization:pelvis	0 0 0 0 ( 0) ( 0) ( 0) ( 0)		0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 0 0 0 (7)(0)(0)(0)
	mineralization:cortex	0 0 0 0 (0)(0)(0)(0)		0 0 0 0 (0)(0)(0)(0)(0)	1 0 0 0 (4)(0)(0)(0)
rin bladd	simple hyperplasia:transitional epitheliu	<10> um 0 0 0 0 ( 0) ( 0) ( 0) ( 0		0       0       0       0         (       0)       (       0)       (       0)	<27> 0 1 0 0 ( 0) ( 4) ( 0) ( 0)

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

PAGE : 11

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

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Organ	Findings	Group Name         0 ppm           No. of Animals on Study         10           Grade         1         2         3         4	3 ppm 8 <u>1 2 3 4</u> (%) (%) (%) (%)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	30 ppm 27 <u>1 2 3 4</u> (%) (%) (%) (%)
{Endocrine s	ystem)				
pituitary	cyst	<10> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 1 0 0 0 (13) (0) (0) (0)	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<27> 1 0 0 0 ( 4) ( 0) ( 0) ( 0)
	hyperplasia	1 0 0 0 (10) ( 0) ( 0) ( 0)	2 0 0 0 (25) ( 0) ( 0) ( 0)	1 1 0 0 (8) (8) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	Rathke pouch	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (13) (0) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 1 0 0 ( 4) ( 4) ( 0) ( 0)
	focal hypertrophy	1 0 0 0 (10) (0) (0) (0)	1 1 0 0 (13) (13) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 1 0 0 ( 4) ( 4) ( 0) ( 0)
thyroid	ultimibranchial body remanet	<10> 1 0 0 0 (10) (0) (0) (0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<27> 1 0 0 0 ( 4) ( 0) ( 0) ( 0)
	C-cell hyperplasia	1 0 0 0 (10) (0) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 1 0 ( 0) ( 0) ( 8) ( 0)	1 0 0 0 (4)(0)(0)(0)
	focal follicular cell hyperplasia	1 0 0 0 (10) (0) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 (0)(0)(0)(0)	1 1 0 0 (4)(4)(0)(0)
adrenal	hyperplasia:cortical cell	<10> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	$\begin{array}{c} <12 \\ 1 & 0 & 0 \\ (8) & (0) & (0) & (0) \end{array}$	<27> 1 1 0 0 ( 4) ( 4) ( 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

Prgan	Findings	Group Name         0 ppm           No. of Animals on Study         10           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%)	3 ppm 8 <u>1 2 3 4</u> (%) (%) (%) (%)	10 ppm 12 <u>1 2 3 4</u> (%) (%) (%) (%)	30 ppm 27 <u>1 2 3 4</u> (%) (%) (%) (%)
Andocrine s	ystem)				
drenal	hyperplasia:medulla	<10> 3 0 0 0 ( 30) ( 0) ( 0) ( 0)	< 8> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<12> 1 1 0 0 ( 8) ( 8) ( 0) ( 0)	<27> 1 0 0 0 ( 4) ( 0) ( 0) ( 0)
	focal fatty change:cortex	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 0 0 0 (17) (0) (0) (0)	5 1 0 0 (19) (4) (0) (0)
Reproductiv	e system)				
estis	atrophy	<10> 0 0 3 0 ( 0) ( 0) ( 30) ( 0)	< 8> 1 1 1 0 (13) (13) (13) (0)	<12> 1 2 7 0 ( 8) ( 17) ( 58) ( 0)	<27> 1 2 23 0 ( 4) ( 7) ( 85) ( 0)
	mineralization	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	3 0 0 0 (25)(0)(0)(0)	2 0 0 0 (7)(0)(0)(0)
	arteritis	0 1 0 0 ( 0) ( 10) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	interstitial cell hyperplasia	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (8)(0)(0)(0)	1 0 0 0 (4)(0)(0)(0)
rostate	inflammation	$\begin{array}{c} <10 \\ 2 & 0 & 1 & 0 \\ (20) & (0) & (10) & (0) \end{array}$	< 8> 1 0 0 0 (13) (0) (0) (0)	<12> 1 1 1 0 ( 8) ( 8) ( 8) ( 0)	$\begin{array}{c} <27 \\ 2 & 1 & 1 & 0 \\ (7) & (4) & (4) & (0) \end{array}$

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

b : Number of animals with lesion ь

(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)

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STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj

| STUDY NO.   | : 0342           |  |
|-------------|------------------|--|
| ANIMAL      | : RAT F344/DuCrj |  |
| REPORT TYPE | : A1             |  |
| SEX         | : MALE           |  |

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| Organ        | Findings         | Group Name         0 ppm           No. of Animals on Study         10           Grade         1         2         3         4           (%)         (%)         (%)         (%) | 3 ppm<br>8<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>12<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>27<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|--------------|------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| Reproductive | system)          |                                                                                                                                                                                 |                                                 |                                                   |                                                   |
| rostate      | hyperplasia      | <10><br>1 0 0 0<br>(10) (0) (0) (0)                                                                                                                                             | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)          | <12><br>2 0 0 0<br>(17) ( 0) ( 0) ( 0)            | <27><br>2 0 0 0<br>( 7) ( 0) ( 0) ( 0)            |
| ammary gl    | duct ectasia     | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)                                                                                                                                         | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)          | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <27><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
|              | galactocele      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                  | 0 0 0 0<br>(0)(0)(0)(0)                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 1 0 0 0<br>(4)(0)(0)(0)                           |
| Nervous syst | tem)             |                                                                                                                                                                                 |                                                 |                                                   |                                                   |
| rain         | hemorrhage       | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                          | < 8><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)          | <12><br>1 0 0 0<br>( 8) ( 0) ( 0) ( 0)            | <27><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 1 0 0<br>( 0) ( 4) ( 0) ( 0                     |
|              | gliosis          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                  | 0 0 0 0<br>(0)(0)(0)(0)                         | 0 1 0 0<br>( 0) ( 8) ( 0) ( 0)                    | 1 0 0 0<br>(4)(0)(0)(0                            |

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

(HPT150)

PAGE: 14

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

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SEX :	MALE			PAGE : 15
Organ	Findings	Group Name         0 ppm           No. of Animals on Study         10           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	30 ppm 27 <u>1 2 3 4</u> (%) (%) (%) (%)
{Nervous syste	em)	•		
spinal cord .	gliosis	<10> 0 0 0 0 . ( 0) ( 0) ( 0)	<12> 0 1 0 0 ( 0) ( 8) ( 0) ( 0)	<27> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
{Special sense	e organs/appendage)			
еуе	hemorrhage	<10> 1 0 0 0 ( 10) ( 0) ( 0) ( 0)	$\begin{array}{cccc} <12> \\ 0 & 0 & 0 & 0 \\ ( & 0) & ( & 0) & ( & 0) & ( & 0) \end{array}$	<27> 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)	0 2 0 0 ( 0) ( 7) ( 0) ( 0)
	retinal atrophy	7 0 0 0 (70)(0)(0)(0)	6 0 0 0 (50)(0)(0)(0)	12 0 2 0 (44) (0) (7) (0)
	keratitis	0 0 0 0 ( 0) ( 0) ( 0) ( 0	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 0 1 0 (7) (0) (4) (0)
	iritis	0 0 0 0 ( 0) ( 0) ( 0) ( 0	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 4) ( 0) ( 0)
Harder gl	degeneration	<10> 1 2 0 0 ( 10) ( 20) ( 0) ( 0	<12> 1 0 0 0 ( 8) ( 0) ( 0) ( 0)	<27> 4 1 0 0 (15) (4) (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

(с) с: b/а\*100

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

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Drgan	No.	рир Name of Animals on Study ade <u>1</u> (%)	0 ppm 10 <u>2 3</u> (%) (%)	<u>4</u> (%)	<u>1</u> 2 (%) (%)	3 ppm 8 <u>3 4</u> (%) (%)	<u> </u>	10 ppm 12 2 <u>3 4</u> %) (%) (%)	<u> </u>	30 ppm 27 <u>2 3</u> (%) (%)	<u>4</u> (%)
{Special sens	e organs/appendage)										
Harder gl	lymphocytic infiltration	0 ( 0) (	<10> 0 0 0) ( 0)	0 ( 0)	<pre></pre>	8> 0 0 ( 0) ( 0)	0 ( 0) (	<12> 0 0 0 0) ( 0) ( 0)	1 ( 4)	<27> 0 0 ( 0) ( 0) (	0 0)
{Musculoskele	tal system)										
ruscle	atrophy	0 ( 0) (	<10> 0 0 0) ( 0)	0 ( 0)	<pre></pre>	8> 0 0 ( 0) ( 0)	0 ( 0) (	<12> 0 0 0 0) ( 0) ( 0)	0 ( 0)	<27> 1 0 ( 4) ( 0) (	0 0)
Body cavitie:	s)										
eritoneum	mesothelial hyperplasia	0 ( 0) (	<10> 0 0 0) ( 0)	0 ( 0)	<pre></pre>	8> 0 0 ( 0) ( 0)	0	<12> 0 0 0 0) ( 0) ( 0)	1 ( 4)	<27> 0 0 ( 0) ( 0) (	0 0)
a> b c)	<pre>1 : Slight 2 : Moderate 3 : Mathematical Action 1 : Slight 2 : Moderate 3 : Mathematical Action 1 : Mumber of animals with lesion 1 : C : D / a * 100 ifference; * : P ≤ 0.05 ** :</pre>	farked 4 : Severe 01 Test of Chi Square									

BAIS3

APPENDIX J 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

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

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rgan	Findings	Group Name No. of Animals on Study Grade	<u>1 2</u> %) (%)	0 ppm 40 3 (%)	<u>4</u> (%)	1(%)		<u>4</u> <u>1</u> (%)	10 ppu 38 <u>2 3</u> (%) (%)	4	<u> </u>	30 ppn 23 <u>2 3</u> (%) (%)	4
Integumentar	v system/appandage)												
kin/app	inflammation		, 0 0 0) ( 0)		0 ( 0)	0 ( 0) (	<42> 1 0 2) ( 0) (	0 0 0) ( 0)	<38> 0 0 ( 0) ( 0)		0 ( 0) (	<23> 1 0 4) ( 0)	
	hyperplasia:epidermis		0 0 0) ( 0)		0 ( 0)	1 ( 2) (	0 0 0) ( 0) (	0 0 0) ( 0)	0 0 ( 0) ( 0)		0 ( 0) (	0 0 0) ( 0)	
	scab		0 0 0) ( 0)		0 ( 0)	1 (2)(	0 0 0) ( 0) (	0 1 0) (3)	00 (0)(0)	0 ) ( 0)	1 ( 4) (	0 0 0) ( 0)	0 ) ( 0)
	epidermal cyst		0 0 0) ( 0)		0 ( 0)	0 ( 0) (	0 0 0) ( 0) (	0 0 0) ( 0)	00 (0)(0)	0 ) ( 0)	1 ( 4) (	0 0 0) ( 0)	
espiratory :	system}												
sal cavit	thrombus		0 0 0) ( 0)		0 ( 0)	0 ( 0) (	<42> 0 0 0) ( 0) (	0 0 0) ( 0)	<38> 1 0 ( 3) ( 0)		0 ( 0) (	<23> 0 0 0) ( 0)	
	mineralization		000 (5) (0)		0 ( 0)	· 31 (74) (	1 0 2)(0)(	0 23 0) ( 61)	00 (0)(0)		18 ( 78) (	0 0 0) ( 0)	
	squamous cell hyperplasia		0 0 0) ( 0)		0 ( 0)	0 ( 0) (	0 0 0) ( 0) (	0 0 0) ( 0)	00 (0)(0)		2 (9)(	2 0 9) ( 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

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

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)rgan	j	Group Name No. of Animals on Study Grade <u>1</u> (%)	0 ppm 40 <u>2 3 4</u> (%) (%) (%)	3 ppm 42 <u>1 2 3 4</u> (%) (%) (%) (%)	10 ppm 38 <u>1 2 3 4</u> (%) (%) (%) (%)	30 ppm 23 <u>1 2 3 4</u> (%) (%) (%) (%)
Respiratory	system)					
asal cavit	eosinophilic change:olfactory epitheli		<40> 17 3 0 (43) (8) (0)	<pre>&lt;42&gt; 23 15 2 0 (55) (36) (5) (0)</pre>	<38> 16 16 4 0 (42) (42) (11) (0)	<23> 16 2 0 0 ** (70) (9) (0) (0)
	eosinophilic change:respiratory epithe		1 0 0 (3)(0)(0)	24 0 0 0 (57)(0)(0)(0)	24 0 0 0 (63)(0)(0)(0)	11 0 0 0 (48) (0) (0) (0)
	inflammation:foreign body	16 ( 40)	1 0 0 (3)(0)(0)	15 1 0 0 (36)(2)(0)(0)	10 2 0 0 (26)(5)(0)(0)	1 1 0 0 *** (4)(4)(0)(0)
	inflammation:squamous epithelium	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)
	inflammation:respiratory epithelium	6 (15)	0 0 0 ( 0) ( 0) ( 0)	5 0 0 0 (12) (0) (0) (0)	5 1 0 0 (13) (3) (0) (0)	5 11 0 0 ** (22)(48)(0)(0)
	respiratory metaplasia:olfactory epith		0 0 0 ( 0) ( 0) ( 0)	3 0 0 0 (7)(0)(0)(0)	1 0 0 0 (3)(0)(0)(0)	2 0 0 0 (9)(0)(0)(0)
	respiratory metaplasia:gland	35 (88)	0 0 0 ( 0) ( 0) ( 0)	41 0 0 0 (98) (0) (0) (0)	37 0 0 0 (97)(0)(0)(0)	22 0 0 0 (96)(0)(0)(0)
	inflammation:transitional epithelium	8 (20)	0 0 0 ( 0) ( 0) ( 0)	15 0 0 0 (36) (0) (0) (0)	3 0 0 0 (8)(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

ANIMAL : REPORT TYPE :	RAI F344/DuCrj	HISTOLOGICAL FINDINGS :NON-NI SACRIFICED ANIMALS (105W)	EOPLASTIC LESIONS (SUMMARY)		
Organ	Group Name No. of Animals on Grade	0 ppm Study 40 <u>1 2 3 4</u> (%) (%) (%) (%)	3 ppm 42 <u>1 2 3 4</u> (%) (%) (%) (%)	10 ppm 38 <u>1 2 3 4</u> (%) (%) (%) (%)	PAGE : $ \begin{array}{r} 30 \text{ ppm} \\ 23 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array} $
Respiratory	system)				
nasal cavit	squamous cell metaplasia:respiratory epithelium	<40> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<42> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<38> 2 0 0 0 (5) (0) (0) (0)	<23> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	squamous cell metaplasia with atypia:respiratory epithel ium	0 0 0 0 (0)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)	1 0 0 0 (3)(0)(0)(0)	5 17 0 0 <b>**</b> (22) (74) (0) (0)
	squamous cell hyperplasia with atypia	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	5 6 0 0 ** (22) (26) (0) (0)
	hyperplasia with atypia:respiratory epithelium	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 0 0 0 (9)(0)(0)(0)
	hyperplasia with atypia:nasal 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 2 0 0 ( 0) ( 9) ( 0) ( 0)
	hyperplasia with atypia:transitional epithelium	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 0 0 0 (5)(0)(0)(0)	1 0 0 0 ( 4) ( 0) ( 0) ( 0)
	hyperplasia:transitional epithelium	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	11 0 0 0 ** (29) (0) (0) (0)	4 0 0 0 * (17) (0) (0) (0)
	atrophy:olfactory epithelium	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	4 0 0 0 * (17) (0) (0) (0)

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

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

(c)

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

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Organ	Findings	Group Name         0 ppm           No. of Animals on Study         40           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%)	$\begin{array}{c} 3 \text{ ppm} \\ 42 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array}$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	30 ppm 23 <u>1 2 3 4</u> (%) (%) (%) (%)
{Respiratory :	system)				- -
nasal cavit	necrosis:respiratory epithelium	<40> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<42> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<23> 1 0 0 0 ( 4) ( 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 0 ( 0) ( 0) ( 0) ( 0)	3 1 0 0 * (13) (4) (0) (0)
	thickening of bone:turbinate	0 0 0 0 (0)(0)(0)(0)	3 0 0 0 (7)(0)(0)(0))	20 11 0 0 ** (53) (29) (0) (0)	7 2 0 0** (30)(9)(0)(0)
larynx	inflammation	<40> 7 0 0 0 (18) (0) (0) (0)	<42> 4 0 0 0 (10) (0) (0) (0)	<38> 11 0 0 0 (29) (0) (0) (0)	<23> 5 1 0 0 (22) (4) (0) (0)
lung	congestion	( 0) ( 0) ( 0) ( 0)	<42> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<23> 0 1 0 0 ( 0) ( 4) ( 0) ( 0)
	accumulation of foamy cells	1 0 0 0 (3) (0) (0) (0)	3 0 0 0 (7)(0)(0)(0)	4 0 0 0 (11) (0) (0) (0)	3 0 0 0 (13)(0)(0)(0)
	bronchiolar—alveolar cell hyperplasi	a 0 1 0 0 ( 0) ( 3) ( 0) ( 0)	2 0 0 0 (5)(0)(0)(0)	1 1 0 0 (3)(3)(0)(0)	1 1 0 0 (4)(4)(0)(0)

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

b b: Number of animals with lesion

(c) c:b/a\*100

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

(HPT150)

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

					PAGE ·	
Organ	Findings	Group Name 0 ppm No. of Animals on Study 40 Grade <u>1 2 3 4</u> (%) (%) (%) (%	3 ppm 42 <u>1 2 3 4</u> (%) (%) (%) (%)	10 ppm 38 <u>1 2 3 4</u> (%) (%) (%) (%)	30 ppm 23 <u>1 2 3 4</u> (%) (%) (%) (%)	
{Hematopoieti	c system)					
bone marrow	angiectasis	<40> 0 0 0 0 ( 0) ( 0) ( 0) ( 0	<42> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<38> 1 1 0 0 ( 3) ( 3) ( 0) ( 0)	<23> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	
	granulation	7 0 0 0 (18) (0) (0) (0	3 0 0 0 (7)(0)(0)(0)	2 1 0 0 (5)(3)(0)(0)	1 0 0 0 (4)(0)(0)(0)	
	increased hematopoiesis	5 0 0 0 (13) (0) (0) (0	2 0 0 0 (5)(0)(0)(0)	3 0 0 0 (8)(0)(0)(0)	1 0 0 0 ( 4) ( 0) ( 0) ( 0)	
	decreased 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)	
	erythropoiesis:increased	0 0 0 0 (0)(0)(0)(0)	1 1 0 0 (2)(2)(0)(0)	1 1 0 0 (3)(3)(0)(0)	3 0 0 0 (13) (0) (0) (0)	
spleen	deposit of hemosiderin	<40> 17 1 0 0 (43) (3) (0) (0		<38> 0 0 0 0 *** ( 0) ( 0) ( 0) ( 0)	<23> 4 0 0 0 (17) (0) (0) (0)	
	fibrosis	0 0 0 0 ( 0) ( 0) ( 0) ( 0	5 0 0 0 (12) (0) (0) (0)	2 0 0 0 (5)(0)(0)(0)	7 0 0 0 ** (30) (0) (0) (0)	
	extramedullary hematopoiesis	18 1 0 0 (45)(3)(0)(0	26 2 1 0 (62) (5) (2) (0)	22 4 0 0 (58) (11) (0) (0)	12 3 0 0 (52)(13)(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

ANIMAL : REPORT TYPE :		/DuCrj HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)				
SEX :	MALE		·		PAGE :	
Organ	Findings	Group Name         0 ppm           No. of Animals on Study         40           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%)	3 ppm 42 <u>1 2 3 4</u> (%) (%) (%) (%)	10 ppm 38 <u>1 2 3 4</u> (%) (%) (%) (%)	30 ppm 23 <u>1 2 3 4</u> (%) (%) (%) (%)	
{Circulatory :	system)					
heart	myocardial fibrosis	<40> 16 23 0 0 (40) (58) (0) (0)	<42> 28 13 0 0 * ( 67) ( 31) ( 0) ( 0)	<38> 22 13 0 0 (58) (34) (0) (0)	<23> 15 8 0 0 (65) (35) (0) (0)	
artery/aort	arteritis	<40> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<42> 0 1 0 0 ( 0) ( 2) ( 0) ( 0)	<38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<23> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	
{Digestive sys	stem)					
tongue	inflammatory infiltration	<40> 1 0 0 0 (3) (0) (0) (0)	<42> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<23> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	
	arteritis	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 0 0 0 (5)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	
stomach	ulcer:forestomach	<40> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<42> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<23> 0 1 0 0 ( 0) ( 4) ( 0) ( 0)	
	hyperplasia:forestomach	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 2) ( 0) ( 0)	1 0 0 0 (3)(0)(0)(0)	0 1 0 0 ( 0) ( 4) ( 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

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

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)rgan	Findings	Group Name 0 ppm No. of Animals on Study 40 Grade <u>1 2 3</u> (%) (%) (%) (	$\begin{array}{c} 3 \text{ ppm} \\ 42 \\ 4 \\ \% \\ \hline (\%) \\ (\%$	10 ppm 38 <u>1 2 3 4</u> (%) (%) (%) (%)	30 ppm 23 <u>1 2 3 4</u> (%) (%) (%) (%)
Digestive	system)				
tomach	erosion:glandular stomach	<40> 3 0 0 (8)(0)(0)(	<42> 0 1 0 0 0 0) (2) (0) (0) (0)	<38> 3 0 0 0 ( 8) ( 0) ( 0) ( 0)	<23> 2 0 0 0 (9) (0) (0) (0)
iver	herniation	<40> 5 0 0 (13) (0) (0) (	<pre>&lt;42&gt; 0 6 0 0 0 0) (14) (0) (0) (0)</pre>	<38> 6 0 0 0 (16) (0) (0) (0)	<23> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	peliosis-like lesion	2 0 0 (5)(0)(0)(	0 0 0 0 0 0) ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 ( 4) ( 0) ( 0) ( 0)
	necrosis:central	0 0 0 ( 0) ( 0) ( 0) (	0 0 0 0 0 0) ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 ( 4) ( 0) ( 0) ( 0)
	necrosis:focal	2 1 0 ( 5) ( 3) ( 0) ( ·	0 2 0 0 0 0) ( 5) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	fatty change	0 0 0 ( 0) ( 0) ( 0) (	0 0 0 0 0 0) ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (3)(0)(0)(0)	2 0 0 0 (9)(0)(0)(0)
	lymphocytic infiltration	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 ( 4) ( 0) ( 0) ( 0)
	granulation	13 1 0 (33) (3) (0) (	0 15 0 0 0 0) (36)(0)(0)(0)	16 0 0 0 (42)(0)(0)(0)	10 0 0 0 (43)(0)(0)(0)

b b : Number of animals with lesion

(c) c:b/a\*100

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

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: MALE				PAGE : 8
Findings	Group Name 0 ppm No. of Animals on Study 40 Grade <u>1 2 3 4</u> (%) (%) (%) (%)	$\begin{array}{c} 3 \text{ ppm} \\ 42 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array}$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
system)				
perivascular inflammation	<40>	<42>	<38>	<23>
	0 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) ( 0) ( 0) ( 0)
extramedullary hematopoiesis	0 0 0 0	2 0 0 0	0 0 0 0	1 0 0 0
	( 0) ( 0) ( 0) ( 0)	(5)(0)(0)(0)	( 0) ( 0) ( 0) ( 0)	(4)(0)(0)(0)
clear cell focus	4 0 0 0	3 1 0 0	10 0 0 0	2 0 0 0
	(10) (0) (0) (0)	(7)(2)(0)(0)	(26)(0)(0)(0)	(9) (0) (0) (0)
acidophilic cell focus	6 1 0 0	16 1 0 0	4 1 0 0	3 0 0 0
	(15) (3) (0) (0)	(38) (2) (0) (0)	(11) (3) (0) (0)	(13) (0) (0) (0)
basophilic cell focus	3 1 0 0	19 0 0 0 ***	15 2 0 0 **	2 0 0 0
	( 8) ( 3) ( 0) ( 0)	(45) (0) (0) (0)	(39)(5)(0)(0)	(9)(0)(0)(0)
spongiosis hepatis	4 0 0 0	3 1 0 0	3 1 0 0	4 0 0 0
	(10) (0) (0) (0)	(7)(2)(0)(0)	(8)(3)(0)(0)	(17) (0) (0) (0)
bile duct hyperplasia	38 2 0 0	41 1 0 0	35 3 0 0	20 3 0 0
	(95)(5)(0)(0)	(98) (2) (0) (0)	(92)(8)(0)(0)	(87) (13) (0) (0)
cholangiofibrosis	0 0 0 0	0 0 0 0	1 0 0 0	0 0 0 0
	( 0) ( 0) ( 0) ( 0)	( 0) ( 0) ( 0) ( 0)	(3)(0)(0)(0)	( 0) ( 0) ( 0) ( 0)
	Findings	Group Name No. of Animals on Study         0 40           Findings         1         2         3         4           Findings         (%)         (%)         (%)         (%)         (%)           system) $(40)^{\circ}$ $(40)^{\circ}$ $(5)^{\circ}$ $(5)^{\circ}$ $(5)^{\circ}$ perivascular inflammation $(0)^{\circ}$ $(1)^{\circ}$ $(0)^{\circ}$ $(0)^{\circ}$ $(0)^{\circ}$ $(0)^{\circ}$ extramedullary hematopoiesis $(0)^{\circ}$ $(0)^{\circ}$ $(0)^{\circ}$ $(0)^{\circ}$ $(0)^{\circ}$ clear cell focus $(10)^{\circ}$ $(0)^{\circ}$ $(0)^{\circ}$ $(0)^{\circ}$ $(0)^{\circ}$ scidophilic cell focus $6$ $1$ $0$ $0$ $(10)^{\circ}$ $(0)^{\circ}$ $(0)^{\circ}$ basophilic cell focus $3$ $1$ $0$ $0$ $(10)^{\circ}$ $(0)^{\circ}$ $($	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$

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:b/a\*100 (c)

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

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

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| Organ                                       | Findings                                                                                                                                                       | Group Name         0 ppm           No. of Animals on Study         40           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $\begin{array}{c} 3 \text{ ppm} \\ 42 \\ \hline 1 & 2 & 3 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 10 \text{ ppm} \\ 38 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $ | 30 ppm<br>23<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|---------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------|---------------------------------------------------|
| {Digestive                                  | system)                                                                                                                                                        |                                                                                                                                                                                             |                                                                                                            |                                                                                                           |                                                   |
| liver                                       | biliary cyst                                                                                                                                                   | <40><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                                                                                                                                                      | <42><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                     | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                    | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
| pancreas                                    | atrophy                                                                                                                                                        | <40><br>2 0 0 0<br>( 5) ( 0) ( 0) ( 0)                                                                                                                                                      | <41><br>2 0 0 0<br>( 5) ( 0) ( 0) ( 0)                                                                     | <38><br>2 0 0 0<br>(5) (0) (0) (0)                                                                        | <23><br>3 0 0 0<br>( 13) ( 0) ( 0) ( 0)           |
| -                                           | islet cell hyperplasia                                                                                                                                         | 1 2 0 0<br>(3)(5)(0)(0)                                                                                                                                                                     | 2 1 0 0<br>(5)(2)(0)(0)                                                                                    | 1 1 0 0<br>(3)(3)(0)(0)                                                                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
| {Urinary sy                                 | rstem)                                                                                                                                                         |                                                                                                                                                                                             |                                                                                                            |                                                                                                           |                                                   |
| kidney                                      | eosinophilic body                                                                                                                                              | <40><br>40 0 0 0<br>(100) ( 0) ( 0) ( 0)                                                                                                                                                    | <42><br>42 0 0 0<br>(100) ( 0) ( 0) ( 0)                                                                   | <38><br>37 0 0 0<br>(97) (0) (0) (0)                                                                      | <23><br>21 0 0 0<br>(91) (0) (0) (0)              |
|                                             | chronic nephropathy                                                                                                                                            | 9 20 11 0<br>(23) (50) (28) (0)                                                                                                                                                             | 6 18 18 0<br>(14) (43) (43) (0)                                                                            | 7 15 16 0<br>(18) (39) (42) (0)                                                                           | 1 8 14 0 *<br>(4)(35)(61)(0)                      |
|                                             | mineralization:papilla                                                                                                                                         | 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)                    |
| Grade<br>< a ><br>b<br>( c )<br>Significant | 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 ≤ 0.05 ** : P | 3 : Marked 4 : Severe<br>site<br>≤ 0.01 Test of Chi Square                                                                                                                                  |                                                                                                            |                                                                                                           |                                                   |

(HPT150)

BAIS3

| SEX :         | MALE                  |                                                             |                                            |                                                  |                                                       | PAGE                                              |
|---------------|-----------------------|-------------------------------------------------------------|--------------------------------------------|--------------------------------------------------|-------------------------------------------------------|---------------------------------------------------|
| Organ         | Findings              | Group Name<br>No. of Animals on Study<br>Grade <u>1</u> (%) | 0 ppm<br>40<br>2 <u>3 4</u><br>(%) (%) (%) | 3 ppm<br>42<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | 30 ppm<br>23<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| {Urinary syst | .em)                  |                                                             |                                            | · · · · · · · · · · · · · · · · · · ·            |                                                       |                                                   |
| Kidney        | mineralization;pelvis | 0<br>( 0) (                                                 | <40><br>0 0 0<br>0) ( 0) ( 0)              | <42><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)           | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
| urin bladd    | xanthogranuloma       | 0<br>( 0) (                                                 | <40><br>0 0 0<br>0) ( 0) ( 0)              | <42><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <38><br>1 0 0 0<br>(3) (0) (0) (0)                    | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
| {Endocrine sy | /stem}                |                                                             |                                            |                                                  |                                                       |                                                   |
| pituitary     | angiectasis           | 0<br>( 0) (                                                 | <40><br>0 0 0<br>0) ( 0) ( 0)              | <42><br>2 0 0 0<br>( 5) ( 0) ( 0) ( 0)           | <38><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                | <23><br>3 0 0 0<br>(13) (0) (0) (0)               |
|               | hemorrhage            | 0<br>( 0) (                                                 | 0 0 0<br>0)(0)(0)                          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|               | cyst                  | 1<br>( 3) (                                                 | 0 0 0<br>0) ( 0) ( 0)                      | 1 0 0 0<br>(2)(0)(0)(0)                          | 2 0 0 0<br>(5)(0)(0)(0)                               | 2 0 0 0<br>(9) (0) (0) (0)                        |
|               | hyperplasia           | 10<br>(25) (                                                | 2 0 0<br>5)(0)(0)                          | 5 2 0 0<br>(12) (5) (0) (0)                      | 5 4 0 0<br>(13) (11) (0) (0)                          | 1 1 0 0<br>(4)(4)(0)(0)                           |

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

(HPT150)

| STUDY NO.   | : | 0342           | HISTOLOGI |
|-------------|---|----------------|-----------|
| ANIMAL      | : | RAT F344/DuCrj | SACRIFICE |
| REPORT TYPE | : | A1             |           |
| SEX         | : | MALE           |           |
|             |   |                |           |

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

| Organ        | Findings                          | Group Name 0 ppm<br>No. of Animals on Study 40<br>Grade <u>1 2 3</u><br>(%) (%) (%) | 3 ppm<br>42<br>(%) 1 2 3 4<br>(%) (%) (%) (%)     | 10 ppm<br>38<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>23<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|--------------|-----------------------------------|-------------------------------------------------------------------------------------|---------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| (Endocrine s | ystem)                            |                                                                                     |                                                   |                                                   |                                                   |
| oituitary    | Rathke pouch                      | <40><br>5 0 0<br>(13) (0) (0) (                                                     | <42><br>0 0 0 0 0<br>0) (0) (0) (0) (0)           | <38><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)            | <23><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)            |
|              | focal hypertrophy                 | 3 0 0<br>(8)(0)(0)(                                                                 | 0 7 0 0 0<br>(17) (0) (0) (0)                     | 4 0 0 0<br>(11) (0) (0) (0)                       | 2 0 0 0<br>(9)(0)(0)(0)                           |
| chyroid      | ultimibranchial body remanet      | <40><br>0 0 0<br>( 0) ( 0) ( 0) (                                                   | <42><br>0 0 0 0 0<br>1 0) ( 0) ( 0) ( 0) ( 0)     | <38><br>2 0 0 0<br>( 5) ( 0) ( 0) ( 0)            | <23><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)            |
|              | C-cell hyperplasia                | 10 0 0<br>(25)(0)(0)                                                                | 0 10 1 0 0<br>(24) (2) (0) (0)                    | 7 1 0 0<br>(18) (3) (0) (0)                       | 3 0 0 0<br>(13) (0) (0) (0)                       |
|              | focal follicular cell hyperplasia | 3 0 0<br>(8)(0)(0)                                                                  | 0 0 1 0 0<br>1 0) ( 0) ( 2) ( 0) ( 0)             | 3 0 0 0<br>(8)(0)(0)(0)                           | 2 1 0 0<br>(9)(4)(0)(0)                           |
| adrenal      | extramedullary hematopoiesis      | <40><br>0 0 0<br>( 0) ( 0) ( 0) (                                                   | <pre>&lt;42&gt; 0 1 0 0 0 0 (2) (0) (0) (0)</pre> | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <23><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)            |
|              | hyperplasia:cortical cell         | 4 0 0<br>(10) (0) (0)                                                               | 0 3 0 0 0<br>( 0) ( 7) ( 0) ( 0) ( 0)             | 3 1 0 0<br>(8)(3)(0)(0)                           | 4 0 0 0<br>(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  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

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

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| <u>эеу</u>   | : MALE                        |                                                                                           |                                                  |                                                   | PAGE : 12                                         |
|--------------|-------------------------------|-------------------------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| Organ        | Findings                      | Group Name 0 ppm<br>No. of Animals on Study 40<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | 3 ppm<br>42<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>38<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>23<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| {Endocrine s | system)                       |                                                                                           |                                                  |                                                   |                                                   |
| adrenal      | hyperplasia:medulla           | <40><br>3 0 0 0<br>( 8) ( 0) ( 0) ( 0)                                                    | <42><br>5 0 0 0<br>(12) (0) (0) (0)              | <38><br>1 1 0 0<br>( 3) ( 3) ( 0) ( 0)            | <23><br>4 0 0 0<br>( 17) ( 0) ( 0) ( 0)           |
|              | focal fatty change:cortex     | 8 1 0 0<br>(20) (3) (0) (0)                                                               | 12 1 0 0<br>(29)(2)(0)(0)                        | 5 0 0 0<br>(13) (0) (0) (0)                       | 5 0 0 0<br>(22)(0)(0)(0)                          |
| {Reproductiv | re system}                    |                                                                                           |                                                  |                                                   |                                                   |
| testis       | atrophy                       | <40><br>1 2 37 0<br>( 3) ( 5) ( 93) ( 0)                                                  | <42><br>2 8 32 0<br>(5) (19) (76) (0)            | <38><br>0 5 33 0<br>( 0) ( 13) ( 87) ( 0)         | <23><br>0 0 23 0<br>( 0) ( 0) (100) ( 0)          |
|              | mineralization                | 5 0 0 0<br>(13)(0)(0)(0)                                                                  | 4 1 0 0<br>(10) (2) (0) (0)                      | 4 0 0 0<br>(11)(0)(0)(0)                          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|              | arteritis                     | 2 0 0 0<br>(5)(0)(0)(0)                                                                   | 2 0 0 0<br>(5)(0)(0)(0)                          | 0 2 0 0<br>(0)(5)(0)(0)                           | 0 1 0 0<br>( 0) ( 4) ( 0) ( 0)                    |
|              | interstitial cell hyperplasia | 3 0 0 0<br>(8)(0)(0)(0)                                                                   | 4 0 0 0<br>(10) (0) (0) (0)                      | 1 0 0 0<br>(3)(0)(0)(0)                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
| semin ves    | inflammation                  | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                    | <42><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)           | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <23><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

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

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

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| rgan            | Findings                                                                                         | Group Name         0 ppm           No. of Animals on Study         40           Grade         1         2         3         4           (%)         (%)         (%)         (%) | 3 ppm<br>42<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{c} 30 \text{ ppm} \\ 23 \\ \underline{1  2  3  4} \\ \underline{(\%)  (\%)  (\%)  (\%)} \end{array} $ |
|-----------------|--------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|-------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------|
| Reproductive    | system}                                                                                          |                                                                                                                                                                                 |                                                  |                                                       |                                                                                                                       |
| rostate         | inflammation                                                                                     | <40><br>7 7 0 0<br>(18) (18) (0) (0)                                                                                                                                            | <42><br>7 8 1 0<br>(17) (19) (2) (0)             | <38><br>7 4 0 0<br>(18) (11) (0) (0)                  | <23><br>7 2 0 0<br>(30) (9) (0) (0)                                                                                   |
|                 | hyperplasia                                                                                      | 11 0 0 0<br>(28) (0) (0) (0)                                                                                                                                                    | 6 1 0 0<br>(14) (2) (0) (0)                      | 13 0 0 0<br>(34)(0)(0)(0)                             | 10 0 0 0<br>(43)(0)(0)(0)                                                                                             |
| ammary gl       | hyperplasia                                                                                      | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                          | <42><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <23><br>0 1 0 0<br>( 0) ( 4) ( 0) ( 0)                                                                                |
|                 | galactocele                                                                                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 1 0 0 0<br>(3)(0)(0)(0)                               | 3 0 0 0<br>(13)(0)(0)(0)                                                                                              |
| lervous syste   | em)                                                                                              |                                                                                                                                                                                 |                                                  |                                                       |                                                                                                                       |
| ain             | gliosis                                                                                          | <40><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                                                                                                                                          | <42><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <23><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)                                                                                |
|                 | vacuolic change:nerve cell                                                                       | 0 0 0 0<br>(0)(0)(0)(0)                                                                                                                                                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 1 0 0 0<br>(3)(0)(0)(0)                               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                        |
| a ><br>b<br>c ) | a : Number of animals examined at the si<br>b : Number of animals with lesion<br>c : b / a * 100 | : Marked 4 : Severe<br>te<br>0.01 Test of Chi Square                                                                                                                            |                                                  |                                                       |                                                                                                                       |

(HPT150)

BAIS3

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

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| Organ        | Findings                 | Group Name         0 ppm           No. of Animals on Study         40           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $\begin{array}{c} 3 \text{ ppm} \\ 42 \\ \hline (\%) (\%) (\%) (\%) (\%) \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | 30 ppm<br>23<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|--------------|--------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|-------------------------------------------------------|---------------------------------------------------|
| Special sens | se organs/appendage}     |                                                                                                                                                                                             |                                                                                       |                                                       |                                                   |
| eye          | cataract                 | <40><br>1 1 3 0<br>( 3) ( 3) ( 8) ( 0)                                                                                                                                                      | <42><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                | <38><br>1 0 1 0<br>( 3) ( 0) ( 3) ( 0)                | <23><br>0 1 0 0<br>( 0) ( 4) ( 0) ( 0)            |
|              | retinal atrophy          | 38 0 2 0<br>(95) (0) (5) (0)                                                                                                                                                                | 42 0 0 0<br>(100) ( 0) ( 0) ( 0)                                                      | 34 0 1 0<br>(89) (0) (3) (0)                          | 22 0 0 0<br>(96)(0)(0)(0)                         |
|              | keratitis                | 1 0 0 0<br>(3)(0)(0)(0)                                                                                                                                                                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                        | 0 0 0 0<br>(0)(0)(0)(0)                               | 1 1 1 0<br>(4)(4)(4)(0)                           |
| arder gl     | degeneration             | <40><br>2 0 0 0<br>( 5) ( 0) ( 0) ( 0)                                                                                                                                                      | <42><br>. 4 0 0 0<br>( 10) ( 0) ( 0) ( 0)                                             | <38><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                | <23><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)            |
|              | lymphocytic infiltration | 2 0 0 0<br>(5)(0)(0)(0)                                                                                                                                                                     | 3 0 0 0<br>(7)(0)(0)(0)                                                               | 2 0 0 0<br>(5)(0)(0)(0)                               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
| mbal gl      | inflammation             | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                      | <42><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                                                | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
| Body cavitie | s)                       |                                                                                                                                                                                             |                                                                                       |                                                       |                                                   |
| eritoneum    | cyst                     | <40><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                      | <42><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                | <38><br>1 0 0 0<br>(3)(0)(0)(0)                       | <23><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |

(c) c:b/a \* 100

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

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

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| 0                       |                                                                   | У                                                                                     | 40                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                   | 42                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | ppm                       |                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |          | 10<br>38 | ) ppm<br>} |                 |          |                |           | 30 p <u>p</u><br>23 | m        |          |
|-------------------------|-------------------------------------------------------------------|---------------------------------------------------------------------------------------|----------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|----------|------------|-----------------|----------|----------------|-----------|---------------------|----------|----------|
| Findings                | Grade                                                             | 1<br>(%)                                                                              | 2<br>(%)                                                       | 3<br>(%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | <u>4</u><br>(%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | <br>(%                                                                                                                                                                                                                                                                               | 5)                                                                                                                                                                                                                                                                                                                | 2<br>(%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 3<br>(%)                  | <u>4</u><br>(%) | (9                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | L<br>6)  | 2        | 3<br>(%)   | <u>4</u><br>(%) | (        | <u>1</u><br>%) | 2<br>(%)  |                     |          | 4<br>(%) |
|                         |                                                                   |                                                                                       |                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                           |                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |          |          |            |                 |          |                |           |                     |          |          |
| peritonitis             | (                                                                 | 0<br>0) (                                                                             | 1                                                              | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0<br>( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                   | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 0                         | 0<br>0)         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |          | 0        | 0          | 0<br>( 0)       |          |                | 0         | (                   |          | 0        |
| mesothelial hyperplasia | (                                                                 | 0<br>0) (                                                                             | 0<br>0) (                                                      | 0<br>0) (                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 0<br>( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 1                                                                                                                                                                                                                                                                                    | ;) (                                                                                                                                                                                                                                                                                                              | 0<br>0) (                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 0<br>0) (                 | 0<br>0)         | ( (                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |          | 0<br>0)  | 0<br>( 0)  | 0<br>( 0)       |          |                | 0<br>( 0) |                     |          | 0<br>0   |
| ]                       | peritonitis<br>mesothelial hyperplasia<br>: Slight 2 : Moderate 3 | peritonitis (<br>mesothelial hyperplasia (<br>: Slight 2 : Moderate 3 : Marked 4 : Se | peritonitis 0<br>( 0) (<br>mesothelial hyperplasia 0<br>( 0) ( | veritonitis       0       1         (0)       (3)       (0)         mesothelial hyperplasia       0       0         (0)       (0)       (0)         (0)       (0)       (0)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (2)       (1)       (1)         (2)       (1)       (1)         (2)       (1)       (1)         (2)       (1)       (1)         (2)       (1)       (1)         (2)       (1)       (1)         (2)       (1)       (1)         (2)       (1)       (1)         (2)       (1)       (1)         (2)       (1)       (1)         (2)       (1)       (1)         (2)       (1)       (1)         (2)       (1)       (1)         (2) | veritonitis       (40)         0       1       0         (0)       (3)       (0)         mesothelial hyperplasia       0       0         (0)       (0)       (0)         (0)       (0)       (0)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       (1)         (1)       (1)       ( | veritonitis       (40)         0       1       0       0         (0)       (3)       (0)       (0)         mesothelial hyperplasia       0       0       0         (0)       (0)       (0)       (0)       (0)         : Slight       2 : Moderate       3 : Marked       4 : Severe | veritonitis       (40>)         0       1       0       0         (0)       (3)       (0)       (0)       (0)         mesothelial hyperplasia       0       0       0       1         (0)       (0)       (0)       (0)       (0)       (1)         : Slight       2 : Moderate       3 : Marked       4 : Severe | <40>         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       1       0       0       0       1       0       0       0       1       0       0       0       1       0       0       0       1       0       0       0       1       0       0       0       1       0       0       0       1       0       0       0       1       0       0       0       1       0       0       0       1       0       0       0       1       0       0       0       1       0       0       0       1       0       0       0       0       1       0       0       0       1       0       1       0       0       1       0       1       0       1       0       1       0       1       1       1       1       1 <td>&lt;40&gt;       &lt;40&gt;       &lt;42</td> 0       1       0       0       0       0       0         mesothelial hyperplasia       0       0       0       0       1       0       0       0       0         : Slight       2 : Moderate       3 : Marked       4 : Severe       4 : Severe       4 : Severe | <40>       <40>       <42 | Findings        | Findings       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%)       (%) | Findings | Findings | Findings   | Findings        | Findings | Findings       | Findings  | Findings            | Findings | Findings |

(HPT150)

BAIS3

APPENDIX J 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE: ALL ANIMALS

(2-YEAR STUDY)

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

| Organ        | Findings                  | Group Name         0 ppm           No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | 3 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>49<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|--------------|---------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| Integumentar | y system/appandage}       |                                                                                                                                                                                             |                                                  |                                                   |                                                   |
| kin/app      | hyperplasia:epidermis     | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                      | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <49><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)            | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)            |
|              | scab                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 1 0 0 0<br>(2)(0)(0)(0)                           |
| ubcutis      | inflammation              | <50><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                                                                                                                                                      | <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)            |
| Respiratory  | system)                   |                                                                                                                                                                                             |                                                  |                                                   |                                                   |
| asal cavit   | thrombus                  | <50><br>0 0 1 0<br>( 0) ( 0) ( 2) ( 0)                                                                                                                                                      | <50><br>0 0 1 0<br>( 0) ( 0) ( 2) ( 0)           | <49><br>0 1 1 0<br>( 0) ( 2) ( 2) ( 0)            | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
|              | mineralization            | 43 0 0 0<br>(86) (0) (0) (0)                                                                                                                                                                | 13 0 0 0 **<br>(26) (0) (0) (0)                  | 21 0 0 0 **<br>(43) (0) (0) (0)                   | 38 0 0 0<br>(76)(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 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 3 0 0 0<br>(6)(0)(0)(0)                           |

(c) c:b/a\*100

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

(HPT150)

BAIS3

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

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| Drgan       | Findings                              | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | 0 ppm<br>50<br><u>2 3 4</u><br>(%) (%) (%) | 3 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>49<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|-------------|---------------------------------------|----------------------------------------------------------------|--------------------------------------------|--------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| Respiratory | system)                               |                                                                |                                            |                                                  |                                                   |                                                   |
| asal cavit  | goblet cell hyperplasia               | 0<br>( 0)                                                      | <50><br>0 0 0<br>( 0) ( 0) ( 0)            | <50><br>1 0 0 0<br>( 2) ( 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)            |
|             | eosinophilic change:olfactory epithel |                                                                | 29 10 0<br>(58) (20) (0)                   | 1 18 30 0 **<br>(2)(36)(60)(0)                   | 2 27 20 0 *<br>(4)(55)(41)(0)                     | 9 37 3 0<br>(18) (74) (6) (0)                     |
|             | eosinophilic change:respiratory epith |                                                                | 6 0 0<br>(12) (0) (0)                      | 36 2 0 0<br>(72) (4) (0) (0)                     | 37 1 0 0<br>(76)(2)(0)(0)                         | 27 2 0 0<br>(54) (4) (0) (0)                      |
|             | inflammation:foreign body             | 4<br>( 8)                                                      | 0 0 0<br>( 0) ( 0) ( 0)                    | 3 0 0 0<br>(6)(0)(0)(0)                          | 1 0 0 0<br>(2)(0)(0)(0)                           | 1 0 0 0<br>(2)(0)(0)(0)                           |
|             | inflammation:respiratory epithelium   | 1<br>( 2)                                                      | 0 0 0<br>( 0) ( 0) ( 0)                    | 1 0 0 0<br>(2)(0)(0)(0)                          | 3 0 0 0<br>(6)(0)(0)(0)                           | 21 5 0 0<br>(42)(10)(0)(0)                        |
|             | inflammation:olfactory epithelium     | 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)                    | 2 0 0 0<br>(4)(0)(0)(0)                           |
|             | respiratory metaplasia:olfactory epit |                                                                | 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)                    | 2 0 0 0<br>(4)(0)(0)(0)                           |
|             | respiratory metaplasia:gland          | 49<br>( 98)                                                    | 0 0 0<br>( 0) ( 0) ( 0)                    | 47 0 0 0<br>(94) (0) (0) (0)                     | 48 0 0 0<br>(98) (0) (0) (0)                      | 49 0 0 0<br>(98) (0) (0) (0)                      |

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

(c)

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

| STUDY NO.   | : | 0342           |
|-------------|---|----------------|
| ANIMAL      | : | RAT F344/DuCrj |
| REPORT TYPE | : | A1             |
| SEX         | : | FEMALE         |

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

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| Organ       | Group Name<br>No. of Animals on<br>Grade                        | Study<br>(%) | 5<br>2<br>(%)   | 0 ppm<br>0<br><u>3</u><br>(%) | 4         |   | 1 (%)      | 2<br>(%  |      | 9pm<br>3<br>%) | 4 (%)     |   | <u>1</u><br>(%) |         | 10 ppr<br>49<br><u>3</u><br>(%) |     | <u>4</u><br>(%) | <u>1</u><br>(%) | 2<br>(%)   | 30 pr<br>50<br>3 | 3         | 4 (%)      |
|-------------|-----------------------------------------------------------------|--------------|-----------------|-------------------------------|-----------|---|------------|----------|------|----------------|-----------|---|-----------------|---------|---------------------------------|-----|-----------------|-----------------|------------|------------------|-----------|------------|
| Respiratory | system)                                                         |              |                 |                               |           |   |            |          |      |                |           |   |                 |         |                                 |     |                 |                 |            |                  |           |            |
| nasal cavit | inflammation:transitional epithelium                            | 6<br>(12)    | <54<br>1<br>(2) | 0                             | 0<br>( 0) | ) | 16<br>(32) | 0        | <50> | 0<br>0) (      | 0 *<br>0) |   | 13<br>27) (     | 0       | 19><br>0<br>( 0)                |     | 0<br>0)         | 7<br>(14)       | 0<br>( 0)  |                  | -         | 0<br>0)    |
|             | squamous cell metaplasia:respiratory epithelium                 | 0<br>( 0)    | 0<br>( 0)       | 0<br>( 0)                     | 0<br>( 0) | ) | 0<br>( 0)  | 0        | ) (  | 0<br>0) (      | 0<br>0)   | ( | 2<br>4) (       | 0<br>0) | 0<br>( 0)                       | ) ( | 0<br>0)         | 6<br>(12)       | 0<br>( 0)  | ) ( (            | )<br>)) ( | 0 *<br>0)  |
|             | squamous cell metaplasia with atypia:respiratory epithe.<br>ium | 1 0<br>(0)   | 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)         | 10<br>(20)      | 26<br>(52) |                  |           | 0 *<br>0)  |
|             | squamous cell hyperplasia with atypia                           | 0<br>( 0)    | 0<br>( 0)       | 0<br>( 0)                     | 0<br>( 0) |   | 0<br>( 0)  | 0<br>( 0 | ) (  | 0<br>0) (      | 0<br>0)   | ( | 0<br>0) (       | 0<br>0) | 0<br>( 0)                       |     | 0<br>0)         | 8<br>(16)       | 2<br>( 4)  | ) ( C            |           | 0 **<br>0) |
|             | hyperplasia:nasal gland                                         | 0<br>( 0)    | 0<br>( 0)       | 0<br>( 0)                     | 0<br>( 0) |   | 0<br>( 0)  | 0<br>( 0 | ) (  | 0<br>0) (      | 0<br>0)   | ( | 0<br>0) (       | 0<br>0) | 0<br>( 0)                       | (   | 0<br>0)         | 1<br>(2)        | 0<br>( 0)  | C<br>( (         |           | 0<br>0)    |
|             | hyperplasia with atypia:nasal gland                             | 0<br>( 0)    | 0               | 0<br>( 0)                     | 0<br>( 0) |   | 0<br>( 0)  | 0<br>( 0 | ) (  | 0<br>0) (      | 0<br>0)   | ( | 0<br>0) (       | 0<br>0) | 0<br>( 0)                       | (   | 0<br>0)         | 1<br>(2)        | 0<br>( 0)  |                  |           | 0<br>0)    |
|             | hyperplasia with atypia:transitional epithelium                 | 0<br>( 0)    | 0               | 0<br>(0)                      | 0<br>( 0) |   | 0<br>( 0)  | 0<br>( 0 | ) (  | 0<br>0) (      | 0<br>0)   | ( | 0<br>0) (       | 0<br>0) | 0<br>( 0)                       | (   | 0<br>0)         | 4<br>(8)        | 0<br>( 0)  | 0<br>( 0         |           | 0<br>0)    |
|             | hyperplasia:transitional epithelium                             | 0<br>( 0)    | 0               | 0<br>( 0)                     | 0<br>( 0) |   | 2<br>( 4)  | 0<br>( 0 | ) (  | 0<br>0) (      | 0<br>0)   | ( | 8<br>6) (       | 0<br>0) | 0<br>( 0)                       | (   | 0 **<br>0)      | 13<br>(26)      | 2<br>( 4)  | 0<br>( 0         |           | 0 **<br>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

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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| Organ                                         | 1                                                                                                             | Group Name 0 ppm<br>No. of Animals on Study 50<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | 3 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>49<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|-----------------------------------------------|---------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| {Respiratory                                  | system)                                                                                                       |                                                                                           |                                                  |                                                   |                                                   |
| nasal cavit                                   | atrophy:olfactory epithelium                                                                                  | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | <49><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <50><br>12 1 0 0 **<br>(24) (2) (0) (0)           |
|                                               | necrosis:olfactory epithelium                                                                                 | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 2 0 0 0<br>(4)(0)(0)(0)                           |
|                                               | necrosis:respiratory epithelium                                                                               | 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)                           | 3 1 0 0<br>(6)(2)(0)(0)                           |
|                                               | thickening of bone:turbinate                                                                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 17 0 0 0 ***<br>(35) (0) (0) (0)                  | 20 22 0 0 **<br>(40) (44) (0) (0)                 |
| larynx                                        | inflammation                                                                                                  | <50><br>13 0 0 0<br>(26) (0) (0) (0)                                                      | <50><br>11 0 0 0<br>(22) (0) (0) (0)             | <49><br>15 2 0 0<br>(31) (4) (0) (0)              | <50><br>13 0 0 0<br>(26) (0) (0) (0)              |
| lung                                          | congestion                                                                                                    | <50><br>0 4 0 0<br>( 0) ( 8) ( 0) ( 0)                                                    | <50><br>0 7 0 0<br>( 0) ( 14) ( 0) ( 0)          | <49><br>0 2 0 0<br>( 0) ( 4) ( 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<br>( 0) ( 0) ( 0) ( 0)                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 2 0 0 0<br>(4)(0)(0)(0)                           |
| Grade<br>< a ><br>b<br>( c )<br>Significant d | <pre>s : Number of animals examined at the si<br/>b : Number of animals with lesion<br/>c : b / a * 100</pre> |                                                                                           |                                                  |                                                   |                                                   |

(HPT150)

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

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| Organ          | Findings                                                                                             | Group Name         0           No. of Animals on Study         50           Grade         1         2           (%)         (%) | ppm<br><u>3 4</u><br>(%) (%) | 3 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>49<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 30 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ |
|----------------|------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|------------------------------|--------------------------------------------------|---------------------------------------------------|----------------------------------------------------------------------------------------------------------------------|
| {Respiratory   | system)                                                                                              |                                                                                                                                 |                              |                                                  |                                                   |                                                                                                                      |
| lung           | edema                                                                                                | <50<br>0 1<br>( 0) ( 2) (                                                                                                       | 0 0                          | <50><br>0 2 0 0<br>( 0) ( 4) ( 0) ( 0)           | <49><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                               |
|                | inflammation                                                                                         | 0 0<br>( 0) ( 0) (                                                                                                              | 0 0<br>0) ( 0)               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 1 0 0 0<br>(2)(0)(0)(0)                           | 0 0 1 0<br>( 0) ( 0) ( 2) ( 0)                                                                                       |
|                | foreign body granuloma                                                                               | 1 0<br>(2)(0)(                                                                                                                  | 0 0<br>0) ( 0)               | 0 0 0 0 · · · · · · · · · · · · · · · ·          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                       |
|                | accumulation of foamy cells                                                                          | 2 0<br>(4) (0) (                                                                                                                | 0 0<br>0) ( 0)               | 5 0 0 0<br>(10) (0) (0) (0)                      | 1 0 0 0<br>(2)(0)(0)(0)                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                       |
|                | interstitial pneumonia                                                                               | 0 0<br>( 0) ( 0) (                                                                                                              | 0 0<br>0) ( 0)               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 0 0 0 0<br>(0)(0)(0)(0)(0)                        | 1 0 0 0<br>(2)(0)(0)(0)                                                                                              |
|                | bronchiolar-alveolar cell hyperplasia                                                                | 0 0<br>( 0) ( 0) (                                                                                                              | 0 0<br>0) ( 0)               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 2 1 0 0<br>(4)(2)(0)(0)                           | 1 2 0 0<br>(2) (4) (0) (0)                                                                                           |
| {Hematopoietic | c system)                                                                                            |                                                                                                                                 |                              |                                                  |                                                   |                                                                                                                      |
| oone marrow    | granulation                                                                                          | <50<br>8 2<br>(16) (4) (                                                                                                        | 0 0                          | <50><br>6 2 0 0<br>(12) (4) (0) (0)              | <49><br>5 3 0 0<br>(10) (6) (0) (0)               | <50><br>5 0 0 0<br>(10) (0) (0) (0)                                                                                  |
| <a>b</a>       | <pre>a : Number of animals examined at the s b : Number of animals with lesion c : b / a * 100</pre> |                                                                                                                                 |                              |                                                  |                                                   |                                                                                                                      |

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

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| )rgan         | Findings                 | Group Name<br>No. of Animals on Study<br>Grade <u>1</u> (%) | 0 ppm<br>50<br><u>2 3</u><br>(%) (%) | 4           | 5<br>1 <u>2</u><br>%) (%) | 3 ppm<br>0<br><u>3 4</u><br>(%) (%) | 1 (%)        | 10 pp<br>49<br>2 3<br>(%) (%) | 4           | <u> </u>    | 30<br>50<br><u>2</u><br>(%) | ) ppm<br>3<br>(%) | 4 (%)       |
|---------------|--------------------------|-------------------------------------------------------------|--------------------------------------|-------------|---------------------------|-------------------------------------|--------------|-------------------------------|-------------|-------------|-----------------------------|-------------------|-------------|
| Hematopoietio | system}                  |                                                             |                                      |             |                           |                                     |              |                               |             |             |                             |                   |             |
| one marrow    | proliferation:histiocyte | 0<br>( 0)                                                   | <50><br>0 0<br>( 0) ( 0)             |             | 0 0                       | ;0><br>0 0<br>( 0) ( 0)             | 0<br>( 0) (  | <49><br>0 0<br>0) ( 0         |             | 0           | <50<br>0<br>( 0) (          | 1                 | 0<br>(0)    |
|               | increased hematopoiesis  | 4                                                           | 1 0<br>(2) (0)                       |             | 2 1<br>4) (2)             | 0 0<br>(0)(0)                       | 2<br>( 4) (  | 0 0<br>0) ( 0                 |             | 6<br>(12) ( | 2<br>( 4) (                 | 0<br>( 0) (       | 0<br>( 0)   |
|               | myelofibrosis            | 0<br>( 0)                                                   | 0 0<br>(0)(0)                        | 0<br>( 0) ( | 0 1<br>0) (2)             | 0 0<br>( 0) ( 0)                    | 0<br>( 0) (  | 0 0<br>0) ( 0                 | 0<br>) ( 0) | 0<br>( 0) ( | 0<br>( 0) (                 | 0<br>( 0) (       | 0<br>( 0)   |
|               | erythropoiesis:increased | 1<br>( 2)                                                   | 0 0<br>(0)(0)                        | 0<br>( 0) ( | 2 1<br>4) (2)             | 0 0<br>(0)(0)                       | 2<br>( 4) (  | 0 0<br>0) ( 0                 |             | 3<br>(6)    | 3<br>(6)(                   | 0<br>( 0) (       | 0<br>( 0)   |
|               | granulopoiesis:increased | 0<br>( 0)                                                   | 0 0<br>(0)(0)                        |             | 0 0<br>0) ( 0)            | 0 0<br>( 0) ( 0)                    | 0<br>( 0) (  | 1 0<br>2) ( 0                 |             | 0           | 2<br>(4) (                  | 0<br>( 0) (       | 0<br>( 0)   |
| hymus         | cyst                     | 2<br>( 4)                                                   | <50><br>0 0<br>( 0) ( 0)             | 0<br>( 0) ( | 3 0                       | 50><br>0 0<br>( 0) ( 0)             | 0<br>( 0) (  | <49><br>0 0<br>0) ( 0         |             | 2<br>( 4)   | <50<br>0<br>( 0) (          | 0                 | 0<br>( 0)   |
| pleen         | deposit of hemosiderin   | 40<br>( 80)                                                 | <50><br>0 0<br>( 0) ( 0)             |             | 1 0                       | 50><br>0 0<br>( 0) ( 0)             | 41<br>(84) ( | <49><br>1 (<br>2) ( (         |             | 28<br>(56)  | <50<br>0<br>( 0) (          | 0                 | 0 ;<br>( 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

(HPT150)

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

<u>\_\_\_</u>

| )rgan         | Findings                     | Group Name         0 ppm           No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%) | 3 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>49<br><u>1 2 3 4</u><br>(%) (%) (%) (%)          | 30 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|---------------|------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|------------------------------------------------------------|---------------------------------------------------|
| (Hematopoieti | c system)                    |                                                                                                                                                                                 |                                                  |                                                            |                                                   |
| spleen        | fibrosis                     | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                          | <50><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)           | <49><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
|               | extramedullary hematopoiesis | 30 9 1 0<br>(60)(18)(2)(0)                                                                                                                                                      | 34 7 1 0<br>(68) (14) (2) (0)                    | 37 6 0 0<br>(76) (12) (0) (0)                              | 24 7 6 0<br>(48) (14) (12) (0)                    |
| Circulatory   | system)                      |                                                                                                                                                                                 |                                                  |                                                            |                                                   |
| eart          | thrombus                     | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                          | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <49><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | <50><br>1 0 1 0<br>(2) (0) (2) (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)                                 | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|               | inflammatory cell nest       | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                                                                           | 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)                           |
|               | myocardial fibrosis          | 20 3 0 0<br>(40)(6)(0)(0)                                                                                                                                                       | 26 1 0 0<br>(52)(2)(0)(0)                        | 28 1 0 0<br>(57)(2)(0)(0)                                  | 26 2 0 0<br>(52)(4)(0)(0)                         |
| rtery/aort    | arteritis                    | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                          | <50><br>0 0 1 0<br>( 0) ( 0) ( 2) ( 0)           | <pre> &lt;49&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre> | <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

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

STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

FEMALE SEX

|             |                           | Group Name 0 ppm<br>No. of Animals on Study 50<br>Grade 1 2 3 4           | 3 ppm<br>50<br>1 2 3 4                            | 10 ppm<br>49<br>1 2 3 4                     | 30 ppm<br>50<br>1 2 3 4                |
|-------------|---------------------------|---------------------------------------------------------------------------|---------------------------------------------------|---------------------------------------------|----------------------------------------|
| gan         | Findings                  | Grade $1$ $2$ $3$ $4$ (%)         (%)         (%)         (%)         (%) | $     \frac{1  2  3  4}{(\%)  (\%)  (\%)  (\%)} $ | $\frac{1  2  3  4}{(\%)  (\%)  (\%)  (\%)}$ | <u>1 2 3 4</u><br>(%) (%) (%) (%)      |
| )igestive : | system)                   |                                                                           |                                                   |                                             |                                        |
| ooth        | inflammation              | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                    | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)            | <49><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0)      | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
| ongue       | arteritis                 | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                    | <50><br>5 0 0 0<br>(10) (0) (0) (0)               | <49><br>4 0 0 0<br>(8) (0) (0) (0)          | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0  |
| emach       | mineralization            | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                    | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <49><br>0 2 0 0<br>( 0) ( 4) ( 0) ( 0)      | <50><br>0 0 0 0<br>(0) (0) (0) (0      |
|             | inflammatory infiltration | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                            | 1 1 0 0<br>(2)(2)(0)(0)                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | 0 0 0 0<br>(0)(0)(0)(0)                |
|             | erosion:forestomach       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                            | 0 0 0 0<br>(0)(0)(0)(0)(0)                        | 0 1 0 0<br>(0)(2)(0)(0)                     | 1 0 0 0<br>(2)(0)(0)(0)                |
|             | ulcer:forestomach         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                            | 0 0 0 0<br>(0)(0)(0)(0)(0)                        | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)              | 0 0 0 0<br>(0)(0)(0)(0)                |
|             | hyperplasia:forestomach   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 0 2 0 0<br>( 0) ( 4) ( 0) ( 0)              | 1 1 0 0<br>(2)(2)(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)

|                | 0342<br>RAT F344/DuCrj<br>A1  | HISTOLOGICAL FINDINGS :NON-<br>ALL ANIMALS (0-105W)                                                         | VEOPLASTIC LESIONS (SUMMARY)           |                                        |                                                                        |
|----------------|-------------------------------|-------------------------------------------------------------------------------------------------------------|----------------------------------------|----------------------------------------|------------------------------------------------------------------------|
| SEX :          | FEMALE                        |                                                                                                             |                                        |                                        | PAGE : 28                                                              |
|                |                               | Group Name 0 ppm<br>No. of Animals on Study 50<br>Grade 1 2 3 4                                             | 3 ppm<br>50<br>1 2 3 4                 | 10 ppm<br>49<br><u>1 2 3 4</u>         | 30 ppm<br>50<br>1 2 3 4                                                |
| Organ          | Findings                      | Orace         1         2         3         4           (%)         (%)         (%)         (%)         (%) | (%) (%) (%)                            | (%) (%) (%) (%)                        | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}  (\%)$ |
| {Digestive sys | stem)                         |                                                                                                             |                                        |                                        |                                                                        |
| stomach        | erosion:glandular stomach     | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                                      | <50><br>1 1 0 0<br>( 2) ( 2) ( 0) ( 0) | <49><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0) | <50><br>2 0 0 0<br>(4) (0) (0) (0)                                     |
|                | hyperplasia:glandular stomach | 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)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                         |
| small intes    | erosion                       | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                      | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <49><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0) | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                 |
| liver          | herniation                    | <50><br>15 0 0 0<br>(30) (0) (0) (0)                                                                        | <50><br>4 0 0 0 *<br>(8) (0) (0) (0)   | <49><br>14 0 0 0<br>(29) (0) (0) (0)   | <50><br>4 0 0 0 *<br>( 8) ( 0) ( 0) ( 0)                               |
|                | peliosis-like lesion          | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                                                                              | 1 0 0 0<br>(2)(0)(0)(0)                | 2 0 0 0<br>(4)(0)(0)(0)                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                         |
|                | necrosis:central              | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                                                                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 3 0 0 0<br>(6)(0)(0)(0)                                                |
|                | necrosis:focal                | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                                                                              | 5 1 0 0<br>(10) (2) (0) (0)            | 4 1 0 0<br>(8)(2)(0)(0)                | 6 1 0 0<br>(12) (2) (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) ALL ANIMALS (0-105W)

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|           |                              | Group Name O ppm                                                      | 3 ppm                                   | 10 ppm                                  | 30 ppm                                  |
|-----------|------------------------------|-----------------------------------------------------------------------|-----------------------------------------|-----------------------------------------|-----------------------------------------|
| Organ     | Findings                     | No. of Animals on Study 50<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | 50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 49<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| Digestive | system)                      |                                                                       |                                         |                                         |                                         |
| liver     | fatty change                 | <50><br>1 0 0 0<br>( 2) ( 0) ( 0)                                     | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0)  | <49><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <50><br>2 0 0 0<br>(4)(0)(0)(0)         |
|           | inflammatory infiltration    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0                                         | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)          |
|           | lymphocytic infiltration     | 1 1 0 0<br>(2)(2)(0)(0                                                |                                         | 2 0 0 0<br>(4)(0)(0)(0)                 | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)          |
|           | granulation                  | 28 2 0 0<br>(56)(4)(0)(0                                              |                                         | 23 4 0 0<br>(47)(8)(0)(0)               | 12 4 0 0 **<br>(24) (8) (0) (0)         |
|           | organization                 | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0                                         |                                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)          |
|           | perivascular inflammation    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0                                         |                                         | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)          |
|           | fibrosis:focal               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0                                         |                                         | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)          |
|           | extramedullary hematopoiesis | 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)          |
|           |                              |                                                                       |                                         |                                         |                                         |

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

 $\langle \, a \, \rangle \qquad \ \ a$  : 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) ALL ANIMALS (0-105W)

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|              |                        | Group Name 0 ppm<br>No. of Animals on Study 50                                                                                                           | 3 ppm                                                 | 10 ppm                                                | 30 ppm                                  |
|--------------|------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|-------------------------------------------------------|-----------------------------------------|
| rgan         | Findings               | No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | 50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| Digestive s  | ystem)                 |                                                                                                                                                          |                                                       |                                                       |                                         |
| iver         | clear cell focus       | <50><br>1 0 0 0<br>(2) (0) (0) (0)                                                                                                                       | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <49><br>6 1 0 0<br>(12) (2) (0) (0)                   | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|              | acidophilic cell focus | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                                                    | 2 1 0 0<br>( 4) ( 2) ( 0) ( 0)                        | 5 1 0 0<br>(10) (2) (0) (0)                           | 6 1 0 0<br>(12) (2) (0) (0)             |
|              | basophilic cell focus  | 34 3 0 0<br>(68)(6)(0)(0)                                                                                                                                | 29 9 0 0<br>(58)(18)(0)(0)                            | 33 4 0 0<br>(67) (8) (0) (0)                          | 30 4 0 0<br>(60)(8)(0)(0)               |
|              | bile duct hyperplasia  | 33 0 0 0<br>(66) ( 0) ( 0) ( 0)                                                                                                                          | 31 1 0 0<br>(62)(2)(0)(0)                             | 36 1 0 0<br>(73)(2)(0)(0)                             | 29 0 0 0<br>(58)(0)(0)(0)               |
|              | cholangiofibrosis      | 0 0 1 0<br>( 0) ( 0) ( 2) ( 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)          |
| ancreas      | atrophy                | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0                                                                                                                    | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                | <49><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0)  |
|              | islet cell hyperplasia | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0                                                                                                                            | 1 1 0 0<br>( 2) ( 2) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)          |
| {Urinary sys | stem)                  |                                                                                                                                                          |                                                       |                                                       |                                         |
| tidney       | infarct                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0                                                                                                                    |                                                       | <49><br>1 0 0 0<br>(2) (0) (0) (0)                    | <50><br>0 1 0 0<br>( 0) ( 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

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| Organ        | Findings                             | Group Name         0 ppm           No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%) | 3 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>49<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |  |  |  |
|--------------|--------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------|-------------------------------------------------------|--|--|--|
| {Urinary sys | tem)                                 |                                                                                                                                                                                 |                                                  |                                                   |                                                       |  |  |  |
| kidney       | cyst                                 | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                                                                                                          | <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)                |  |  |  |
|              | hyaline droplet                      | 48       0       0       0         (96)       (0)       (0)       (0)       (0)                                                                                                 | 48 0 0 0<br>(96)(0)(0)(0)                        | 46 0 0 0<br>(94) (0) (0) (0)                      | 48 0 0 0<br>(96)(0)(0)(0)                             |  |  |  |
|              | inflammatory infiltration            | 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)                        |  |  |  |
|              | chronic nephropathy                  | 32 6 0 0<br>(64) (12) (0) (0)                                                                                                                                                   | 25 9 6 0<br>(50) (18) (12) (0)                   | 26 10 3 0<br>(53)(20)(6)(0)                       | 28 10 3 0<br>(56)(20)(6)(0)                           |  |  |  |
|              | hydronephrosis                       | 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)                    | 1 0 0 0<br>(2)(0)(0)(0)                               |  |  |  |
|              | papillary necrosis                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 1 0 0 0<br>(2)(0)(0)(0)                               |  |  |  |
|              | mineralization:cortico-medullary jun | ction 1 0 0 0<br>(2)(0)(0)(0)                                                                                                                                                   | 2 0 0 0<br>(4)(0)(0)(0)                          | 3 0 0 0<br>(6)(0)(0)(0)                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |  |  |  |
|              | mineralization:papilla               | 2 0 0 0<br>(4)(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)                        |  |  |  |

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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| )rgan                  | Group<br>No. o<br>Grade<br>Findings                                                                                                                                             | Name         0 ppm           £ Animals on Study         50           1         2         3         4           (%)         (%)         (%)         (%) | 3 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>49<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| Urinary syst           | em)                                                                                                                                                                             |                                                                                                                                                        |                                                  |                                                   |                                                   |
| idney                  | mineralization:pelvis                                                                                                                                                           | <50><br>9 0 0 0<br>(18) (0) (0) (0)                                                                                                                    | <50><br>2 0 0 0<br>(4) (0) (0) (0)               | <49><br>1 0, 0 0 *<br>( 2) ( 0) ( 0) ( 0)         | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0)            |
|                        | mineralization:cortex                                                                                                                                                           | 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 1 0 0<br>(2)(2)(0)(0)                           |
|                        | atypical tubule hyperplasia                                                                                                                                                     | 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)                    |
| rin bladd              | simple hyperplasia:transitional epithelium                                                                                                                                      | <50><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                                                                                                                 | <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 1 0 0<br>( 0) ( 2) ( 0) ( 0)            |
| Indocrine s            |                                                                                                                                                                                 |                                                                                                                                                        |                                                  |                                                   |                                                   |
| tuitary                | angiectasis                                                                                                                                                                     | <50><br>3 2 0 0<br>( 6) ( 4) ( 0) ( 0)                                                                                                                 | <50><br>7 2 1 0<br>(14) (4) (2) (0)              | <49><br>0 6 1 0<br>( 0) ( 12) ( 2) ( 0)           | <50><br>5 1 0 0<br>(10) (2) (0) (0)               |
|                        | cyst                                                                                                                                                                            | 13 8 2 0<br>(26) (16) (4) (0)                                                                                                                          | 19 7 2 0<br>(38) (14) (4) (0)                    | 18 9 0 0<br>(37)(18)(0)(0)                        | 20 13 2 0<br>(40) (26) (4) (0)                    |
| rade<br>a ><br>b<br>c) | 1 : Slight 2 : Moderate 3 : Man<br>a : Number of animals examined at the site<br>b : Number of animals with lesion<br>c : b / a * 100<br>difference ; * : P ≤ 0.05 ** : P ≤ 0.0 |                                                                                                                                                        |                                                  |                                                   |                                                   |

(HPT150)

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

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| Organ        | Findings                          | Group Name         0 ppm           No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%) | 3 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>49<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|--------------|-----------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| {Endocrine s | ystem)                            |                                                                                                                                                                                 |                                                  |                                                   |                                                   |
| pituitary    | hyperplasia                       | <50><br>4 4 0 0<br>(8) (8) (0) (0)                                                                                                                                              | <50><br>3 1 0 0<br>(6)(2)(0)(0)                  | <49><br>7 7 0 0<br>(14) (14) ( 0) ( 0)            | <50><br>4 5 1 0<br>(8) (10) (2) (0)               |
|              | Rathke pouch                      | 3 0 0 0<br>(6)(0)(0)(0)                                                                                                                                                         | 1 0 0 0<br>(2)(0)(0)(0)                          | 1 0 0 0<br>(2)(0)(0)(0)                           | 2 0 0 0<br>(4)(0)(0)(0)                           |
|              | focal hypertrophy                 | 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)                    | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                    |
| thyroid      | ultimibranchial body remanet      | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                          | <50><br>1 1 0 0<br>( 2) ( 2) ( 0) ( 0)           | <49><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
|              | C-cell hyperplasia                | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                                                                            | 8 2 0 0<br>(16) (4) (0) (0)                      | 13 0 0 0<br>(27) ( 0) ( 0) ( 0)                   | 9 0 0 0<br>(18) (0) (0) (0)                       |
|              | focal follicular cell hyperplasia | 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)                    | 1 0 0 0<br>(2)(0)(0)(0)                           |
| adrenal      | hemorrhage                        | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                          | <50><br>0 1 1 0<br>( 0) ( 2) ( 2) ( 0)           | <49><br>0 1 0 0<br>( 0) ( 2) ( 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

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) ALL ANIMALS (0-105W)

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|                   | (%) (%) (%)                                                            | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$                                            | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
|-------------------|------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|-------------------------------------------------------|
|                   |                                                                        |                                                                                                             |                                                       |                                                       |
| ke lesion         | <50>                                                                   | <50>                                                                                                        | <49>                                                  | <50>                                                  |
|                   | 23 19 1 0                                                              | 28 11 0 0                                                                                                   | 29 7 0 0 *                                            | 27 6 0 0 **                                           |
|                   | (46) (38) (2) (0)                                                      | (56) (22) (0) (0)                                                                                           | (59) (14) ( 0) ( 0)                                   | (54) (12) (0) (0)                                     |
|                   | 0 0 0 0                                                                | 0 1 0 0                                                                                                     | 0 0 0 0                                               | 0 0 0 0 0                                             |
|                   | ( 0) ( 0) ( 0) ( 0)                                                    | ( 0) ( 2) ( 0) ( 0)                                                                                         | ( 0) ( 0) ( 0) ( 0)                                   | ( 0) ( 0) ( 0) ( 0)                                   |
| ary hematopoiesis | 0 0 0 0                                                                | 0 0 0 0                                                                                                     | 1 0 0 0                                               | 0 0 0 0                                               |
|                   | ( 0) ( 0) ( 0) ( 0)                                                    | ( 0) ( 0) ( 0) ( 0)                                                                                         | (2)(0)(0)(0)                                          | ( 0) ( 0) ( 0) ( 0)                                   |
| cortical cell     | 1 0 0 0                                                                | 0 0 0 0                                                                                                     | 0 2 0 0                                               | 1 5 0 0                                               |
|                   | (2)(0)(0)(0)                                                           | ( 0) ( 0) ( 0) ( 0)                                                                                         | (0)(4)(0)(0)                                          | (2)(10)(0)(0)                                         |
| ∶medulla          | 1 0 0 0                                                                | 2 0 0 0                                                                                                     | 2 0 0 0                                               | 2 1 0 0                                               |
|                   | (2)(0)(0)(0)(0)                                                        | ( 4) ( 0) ( 0) ( 0)                                                                                         | ( 4) ( 0) ( 0) ( 0)                                   | (4)(2)(0)(0)                                          |
| change:cortex     | 8 2 0 0                                                                | 12 1 0 0                                                                                                    | 11 6 0 0                                              | 10 10 1 0 *                                           |
|                   | (16) (4) (0) (0)                                                       | (24)(2)(0)(0)                                                                                               | (22)(12)(0)(0)                                        | (20)(20)(2)(0)                                        |
|                   |                                                                        |                                                                                                             |                                                       |                                                       |
|                   | $\langle 50 \rangle$                                                   | <50>                                                                                                        | <49>                                                  | <50>                                                  |
|                   | 1 $1$ $0$ $0$                                                          | 1 2 0 0                                                                                                     | 1 2 0 0                                               | 2 0 0 0                                               |
|                   | (2) $(2)$ $(0)$ $(0)$                                                  | ( 2) ( 4) ( 0) ( 0)                                                                                         | ( 2) ( 4) ( 0) ( 0)                                   | ( 4) ( 0) ( 0) ( 0)                                   |
| anin              | 2 : Moderate 3 : Mark<br>mals examined at the site<br>mals with lesion | 1 1 0 0<br>(2)(2)(0)(0)<br>2: Moderate 3: Marked 4: Severe<br>mals examined at the site<br>mals with lesion | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  |

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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| rgan         | Findings                       | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | 50<br>2             | ppm<br><u>3 4</u><br>(%) (%) | 3 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>49<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%)               |
|--------------|--------------------------------|----------------------------------------------------------------|---------------------|------------------------------|--------------------------------------------------|---------------------------------------------------|-----------------------------------------------------------------|
| Reproductive | e system)                      |                                                                |                     |                              |                                                  |                                                   |                                                                 |
| terus        | dilatation                     | 0<br>( 0)                                                      | <50><br>0<br>( 0) ( | 00<br>0)(0)                  | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <49><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)            | 、<br>(50)<br>(0)<br>(0)<br>(0)<br>(0)<br>(0)<br>(0)<br>(0)<br>( |
|              | hemorrhage                     | 0<br>( 0)                                                      | 0<br>( 0) (         | 0 0<br>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)                                  |
|              | inflammation                   | 0<br>( 0)                                                      | 0<br>( 0) (         | 0 0<br>0) ( 0)               | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                  |
|              | hyperplasia:epithelium         | 1<br>( 2)                                                      |                     | 0 0<br>0) ( 0)               | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                  |
|              | hyperplasia:gland              | 1<br>( 2)                                                      | 0<br>( 0) (         | 0 0<br>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)                                  |
|              | cystic endometrial hyperplasia | 6<br>(12)                                                      | 2<br>( 4) (         | 0 0<br>0) ( 0)               | 3 2 0 0<br>(6)(4)(0)(0)                          | 3 0 0 0<br>(6)(0)(0)(0)                           | 2 4 0 0<br>( 4) ( 8) ( 0) ( 0)                                  |
| agina        | squamous cell hyperplasia      | 0<br>( 0)                                                      | <50)<br>0<br>( 0) ( | ><br>0 0<br>0) ( 0)          | <50><br>1 0 0 0<br>( 2) ( 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)                          |
| ammary gl    | hyperplasia                    | 1<br>( 2)                                                      | <50)<br>0<br>( 0) ( | ><br>0 0<br>0) ( 0)          | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <49><br>0 2 0 0<br>( 0) ( 4) ( 0) ( 0)            | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                          |

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

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

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

(c)

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

| SEX :        | PEMALE                    |                                                |                                          |                                        |          |                                            |                                             | PAGE :    |
|--------------|---------------------------|------------------------------------------------|------------------------------------------|----------------------------------------|----------|--------------------------------------------|---------------------------------------------|-----------|
| )rgan        | Findings                  | No. of Animals on Study 50<br>Grade <u>1</u> 2 | ppm<br><u>3 4</u> <u>1</u><br>(%) (%) (9 | 3 ppm<br>50<br>2 3 4<br>3) (%) (%) (%) | <u> </u> | 10 ppm<br>49<br>2 <u>3 4</u><br>%) (%) (%) | 30 ppm<br>50<br><u>1 2 3</u><br>(%) (%) (%) | 4         |
| Reproductive | system)                   |                                                |                                          |                                        |          |                                            |                                             |           |
| nammary gl   | galactocele               | <50><br>0 0<br>( 0) ( 0) (                     | 0 0 1                                    | <50><br>0 0 0<br>( 0) ( 0) ( 0)        |          | <49><br>0 0 0<br>0) ( 0) ( 0)              | <50><br>1 0 0<br>( 2) ( 0) ( 0)             | 0<br>( 0) |
| Nervous syst | em}                       |                                                |                                          |                                        |          |                                            |                                             |           |
| orain        | hemorrhage                | <50><br>0 0<br>( 0) ( 0) (                     | 0 0 1                                    | <50><br>0 0 0<br>() ( 0) ( 0) ( 0)     |          | <49><br>0 0 0<br>0) ( 0) ( 0)              | <50><br>1 0 0<br>( 2) ( 0) ( 0)             | 0<br>( 0) |
|              | necrosis:focal            | 0 0<br>( 0) ( 0) (                             | 0 0 (<br>0) ( 0) ( (                     | 0 0 0 0<br>1) ( 0) ( 0) ( 0)           |          | 0 0 0<br>0)(0)(0)                          | 0 1 0<br>(0)(2)(0)                          | 0<br>( 0) |
|              | inflammatory infiltration | 0 0<br>( 0) ( 0) (                             | 0 0 (<br>0) ( 0) ( (                     | ) 0 0 0<br>)) ( 0) ( 0) ( 0)           |          | 1 0 0<br>2) ( 0) ( 0)                      | 1 1 0<br>(2)(2)(0)                          | 0<br>( 0) |
|              | gliosis                   | 0 0<br>( 0) ( 0) (                             | 0 0 2<br>0)(0)(4                         | ; 0 0 0<br>;)(0)(0)(0)                 |          | 0 0 0<br>0)(0)(0)                          | 0 3 0<br>(0)(6)(0)                          | 0<br>( 0) |
| Special sens | e organs/appendage)       |                                                |                                          |                                        |          |                                            |                                             |           |
| eye          | cataract                  | <50><br>0 3<br>( 0) ( 6) (                     | 0 0 0                                    | <50><br>1 1 0<br>1) (2) (2) (0)        |          | <49><br>2 0 0<br>4) ( 0) ( 0)              | <50><br>0 0 0<br>( 0) ( 0) ( 0)             | 0<br>( 0) |

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- (c)
- 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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|            |                          | Group Name 0 ppm<br>No. of Animals on Study 50<br>Grade 1 2 3 4 | 3 ppm<br>50                                                      | 10 ppm<br>49                            | 30 ppm<br>50                                          |
|------------|--------------------------|-----------------------------------------------------------------|------------------------------------------------------------------|-----------------------------------------|-------------------------------------------------------|
| gan        | Findings                 | Grade <u>1 2 3 4</u><br>(%) (%) (%) (%)                         | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$ | <u>1 2 3 4</u><br>(%) (%) (%) (%)       | $\begin{array}{c ccccccccccccccccccccccccccccccccccc$ |
| ecial sens | se organs/appendage}     |                                                                 |                                                                  |                                         |                                                       |
|            | retinal atrophy          | <50><br>42 1 1 0<br>(84) (2) (2) (0)                            | <50><br>40 0 2 0<br>(80) (0) (4) (0)                             | <49><br>44 0 2 0<br>(90) (0) (4) (0)    | <50><br>46 0 0 0<br>(92) (0) (0) (0)                  |
|            | keratitis                | 3 0 0 0<br>(6)(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)                        |
|            | iritis                   | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |
| ler gl     | degeneration             | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                          | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                           | <49><br>2 1 0 0<br>( 4) ( 2) ( 0) ( 0)  | <50><br>4 1 0 0<br>( 8) ( 2) ( 0) ( 0)                |
|            | lymphocytic infiltration |                                                                 | 3 0 0 0<br>(6)(0)(0)(0)                                          | 4 0 0 0<br>(8)(0)(0)(0)                 | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |
|            | granulation              | 3 0 0 0<br>(6)(0)(0)(0)                                         | 1 0 0 0<br>(2)(0)(0)(0)                                          | 1 0 0 0<br>(2)(0)(0)(0)(0)              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |
|            | hyperplasia:mast cell    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)          | 1 0 0 0<br>(2)(0)(0)(0)                               |
| olacr d    | inflammation             | <50><br>22 6 0 0<br>(44) (12) (0) (0)                           | <50><br>13 6 0 0<br>(26) (12) (0) (0)                            | <49><br>8 0 0 0 ★★★<br>(16) (0) (0) (0) | <50><br>4 0 0 0;<br>( 8) ( 0) ( 0) ( 0)               |

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

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) ALL ANIMALS (0-105W)

| Organ                                       |                                                                                                                                                                              |                                   | 3 ppm<br>50<br>4 <u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>49<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|---------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------|----------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| Musculoskel                                 | etal system)                                                                                                                                                                 |                                   |                                                    |                                                   |                                                   |
| oone                                        | osteosclerosis                                                                                                                                                               | <50><br>3 1 1<br>( 6) ( 2) ( 2) ( | <50><br>0 6 0 0 0<br>0) (12) (0) (0) (0)           | <49><br>2 1 0 0<br>( 4) ( 2) ( 0) ( 0)            | <50><br>9 2 0 0<br>(18) (4) (0) (0)               |
| rticulus                                    | arthritis                                                                                                                                                                    | <50><br>0 0 0<br>( 0) ( 0) ( 0) ( | <50><br>0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0)        | <49><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)            | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
| Grade<br>( a ><br>b<br>( c )<br>Gignificant | 1 : Slight 2 : Moderate 3 : M<br>a : Number of animals examined at the site<br>b : Number of animals with lesion<br>c : b / a * 100<br>difference ; * : P ≤ 0.05 ** : P ≤ 0. |                                   |                                                    |                                                   |                                                   |

BAIS3

APPENDIX J 5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

| ANIMAL :<br>REPORT TYPE : |                                            | HISTOLOGICAL FINDINGS :NON-N<br>DEAD AND MORIBUND ANIMALS (O         |                                                  |                                                   |                                                   |
|---------------------------|--------------------------------------------|----------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| SEX :                     | FEMALE                                     |                                                                      |                                                  |                                                   | PAGE : 17                                         |
| Organ                     | Group Name<br>No. of Anim<br>Grade         | 0 ppm<br>nals on Study 9<br>(%) (%) (%) (%) (%)                      | 3 ppm<br>12<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>18<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| {Integumentar             | y system/appandage}                        |                                                                      |                                                  |                                                   |                                                   |
| subcutis                  | inflammation                               | < 9><br>0 1 0 0<br>( 0) ( 11) ( 0) ( 0)                              | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <18><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
| {Respiratory              | system)                                    |                                                                      |                                                  |                                                   |                                                   |
| nasal cavit               | thrombus                                   | 0       0       1       0         (0)       (0)       (11)       (0) | <12><br>0 0 1 0<br>( 0) ( 0) ( 8) ( 0)           | <10><br>0 0 1 0<br>( 0) ( 0) ( 10) ( 0)           | <18><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
|                           | mineralization                             | 6 0 0 0<br>(67)(0)(0)(0)                                             | · 6 0 0 0<br>(50) (0) (0) (0)                    | 8 0 0 0<br>(80)(0)(0)(0)                          | 11 0 0 0<br>(61) (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 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 2 0 0 0<br>(11) (0) (0) (0)                       |
|                           | eosinophilic change:olfactory epithelium   | 4 3 1 0<br>(44) (33) (11) (0)                                        | 1 8 2 0<br>(8) (67) (17) (0)                     | 1 7 2 0<br>(10) (70) (20) (0)                     | 6 10 1 0<br>(33) (56) (6) (0)                     |
|                           | eosinophilic change:respiratory epithelium | 5 0 0 0<br>(56)(0)(0)(0)                                             | 4 0 0 0<br>(33)(0)(0)(0)                         | 5 0 0 0<br>(50) (0) (0) (0)                       | 6 0 0 0<br>(33) (0) (0) (0)                       |
|                           | inflammation:respiratory epithelium        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                       | 1 0 0 0<br>(8)(0)(0)(0)                          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 7 2 0 0 <b>*</b><br>(39) (11) (0) (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 b

c:b/a\*100 (c)

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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|              |                                                         | 0 ppm<br>mals on Study 9               | 3 ppm<br>12                                                      | 10 ppm<br>10                                                           | 30 ppm<br>18                           |  |
|--------------|---------------------------------------------------------|----------------------------------------|------------------------------------------------------------------|------------------------------------------------------------------------|----------------------------------------|--|
| gan          | Grade                                                   | <u>1 2 3 4</u><br>(%) (%) (%) (%)      | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$ | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}  (\%)$ | <u>1 2 3 4</u><br>(%) (%) (%) (%)      |  |
| espiratory s | ystem)                                                  |                                        |                                                                  |                                                                        |                                        |  |
| asal cavit   | inflammation:olfactory epithelium                       | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                           | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                 | <18><br>1 0 0 0<br>( 6) ( 0) ( 0) ( 0) |  |
|              | respiratory metaplasia:gland                            | 8 0 0 0<br>(89)(0)(0)(0)               | 10 0 0 0<br>(83) ( 0) ( 0) ( 0)                                  | 9 0 0 0<br>(90) (0) (0) (0)                                            | 18 0 0 0<br>(100) ( 0) ( 0) ( 0)       |  |
|              | inflammation:transitional epithelium                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 3 0 0 0<br>(25)(0)(0)(0)                                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |  |
|              | squamous cell metaplasia:respiratory epithelium         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                         | 2 0 0 0<br>(11) ( 0) ( 0) ( 0)         |  |
|              | squamous cell metaplasia with atypia:respiratory<br>ium | epithel 0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | 1 0 0 0<br>(10) (0) (0) (0)                                            | 5 10 0 0<br>(28)(56)(0)(0              |  |
|              | squamous cell hyperplasia with atypia                   | 0 0 0 0<br>(0)(0)(0)(0)                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                         | 2 1 0 0<br>(11) (6) (0) (0             |  |
|              | hyperplasia:nasal gland                                 | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 C O O<br>( 0) ( 0) ( 0) ( 0)                                   | 0 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                     | 1 0 0 0<br>(6)(0)(0)(0)                |  |
|              | hyperplasia with atypia:transitional epithelium         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | 0 0 0 0<br>(0)(0)(0)(0)                                                | 2 0 0 0<br>(11) (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

| ANIMAL : RAT F344/DuCrj<br>REPORT TYPE : A1<br>SEX : FEMALE | DE.        | AD AND MORIBUND ANIMALS (0-10 | 5W)   |
|-------------------------------------------------------------|------------|-------------------------------|-------|
|                                                             | Group Name | 0 ppm                         | 3 ppm |

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|              |                                     | Group Name<br>No. of Animals on Study | 0 ppm<br>9                       | 3 ppm<br>12                                                      | 10 ppm<br>10                                                     | 30 ppm<br>18                                |
|--------------|-------------------------------------|---------------------------------------|----------------------------------|------------------------------------------------------------------|------------------------------------------------------------------|---------------------------------------------|
| Organ        | Findings                            | Grade <u>1</u><br>(%)                 | 2 <u>34</u><br>(%)(%)(%)         | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$ | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$ | $\frac{1  2  3  4}{(\%)  (\%)  (\%)  (\%)}$ |
| {Respiratory | system)                             |                                       |                                  |                                                                  |                                                                  |                                             |
| nasal cavit  | hyperplasia:transitional epithelium | 0<br>( 0) (                           | < 9><br>0 0 0<br>( 0) ( 0) ( 0)  | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                           | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)                          | <18><br>1 0 0 0<br>( 6) ( 0) ( 0) ( 0)      |
|              | atrophy:olfactory epithelium        | 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)                                   | 8 1 0 0*<br>(44)(6)(0)(0)                   |
|              | necrosis:olfactory epithelium       | 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)                                   | 2 0 0 0<br>(11) (0) (0) (0)                 |
|              | necrosis:respiratory epithelium     | 0<br>( 0)                             | 0 0 0<br>( 0) ( 0) ( 0)          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | 2 0 0 0<br>(20)(0)(0)(0)                                         | 3 1 0 0<br>(17) (6) (0) (0)                 |
|              | thickening of bone:turbinate        | 0<br>( 0)                             | 0 0 0<br>( 0) ( 0) ( 0)          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | 2 0 0 0<br>(20)(0)(0)(0)                                         | 6 7 0 0 **<br>(33) (39) (0) (0)             |
| larynx       | inflammation                        | 0<br>( 0)                             | < 9><br>0 0 0<br>( 0) ( 0) ( 0)  | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                           | <10><br>2 1 0 0<br>(20) (10) (0) (0)                             | <18><br>5 0 0 0<br>(28) (0) (0) (0)         |
| lung         | congestion                          | 0<br>( 0)                             | < 9><br>4 0 0<br>( 44) ( 0) ( 0) | <12><br>0 7 0 0<br>( 0) ( 58) ( 0) ( 0)                          | <10><br>0 2 0 0<br>( 0) ( 20) ( 0) ( 0)                          | <18><br>0 0 0 0 *<br>( 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

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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| STUDY NO.   | : | 0342           |
|-------------|---|----------------|
| 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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| )rgan         | Findings                 | Group Name         0 ppm           No. of Animals on Study         9           Grade         1         2         3         4           (%)         (%)         (%)         (%) | 3 ppm<br>12<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>18<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|---------------|--------------------------|--|--|---|---|
| Respiratory s | system)                  |  |  |   |   |
| ung           | hemorrhage               | <pre></pre>  | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <18><br>2 0 0 0<br>(11) (0) (0) (0)               |
|               | edema                    | 0 1 0 0<br>( 0) ( 11) ( 0) ( 0)  | 0 2 0 0<br>( 0) ( 17) ( 0) ( 0)                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|               | inflammation             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 1 0 0 0<br>(10) (0) (0) (0)                       | 0 0 1 0<br>( 0) ( 0) ( 6) ( 0)                    |
|               | interstitial pneumonia   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 1 0 0 0<br>(6)(0)(0)(0)                           |
| Hematopoieti  | c system)                |  |  |   |   |
| one marrow    | granulation              | <pre>&lt; 9&gt; 1 0 0 0 ( 11) ( 0) ( 0) ( 0)</pre>   | <12><br>1 0 0 0<br>( 8) ( 0) ( 0) ( 0)           | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)           | <18><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
|               | proliferation:histiocyte | 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 1 0<br>( 0) ( 0) ( 6) ( 0)                    |
|               | increased hematopolesis  | 1 0 0 0<br>(11)(0)(0)(0)   | 0 1 0 0<br>( 0) ( 8) ( 0) ( 0)                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 1 2 0 0<br>(6)(11)(0)(0)                          |

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

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| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{pmatrix} < 12 \\ 0 & 1 & 0 & 0 \\ ( & 0) & ( & 8) & ( & 0) & ( & 0) \\ 1 & 1 & 0 & 0 \\ ( & 8) & ( & 8) & ( & 0) & ( & 0) \\ 0 & 0 & 0 & 0 & 0 \\ ( & 0) & ( & 0) & ( & 0) & ( & 0) \\ \end{pmatrix}$ | $\begin{pmatrix} <10 \\ 0 \\ 0 \\ 0 \end{pmatrix} \begin{pmatrix} 0 $ | $(18) \\ 0 & 0 & 0 & 0 \\ ( & 0) & ( & 0) & ( & 0) & ( & 0) \\ 2 & 3 & 0 & 0 \\ ( & 11) & ( & 17) & ( & 0) & ( & 0) \\ 0 & 2 & 0 & 0 \\ ( & 0) & ( & 11) & ( & 0) & ( & 0) \\ \end{array}$ |
|--|---|---|--|
| eased 0 0 0 0<br>(11) (0) (0) (0)<br>eased 0 0 0     | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$   | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | $\begin{array}{cccccccccccccccccccccccccccccccccccc$   |
| (11) (0) (0) (0)<br>eased 0 0 0                      | (8)(8)(0)(0)  | (10) (0) (0) (0)<br>0 1 0 0   | (11) (17) (0) (0<br>0 2 0 0  |
|  |   |   |  |
|  |   |   |  |
| rin 5 0 0 0<br>(56) (0) (0) (0)                      | <12><br>8 0 0 0<br>(67) (0) (0) (0)   | <10><br>6 1 0 0<br>(60) (10) (0) (0)  | <18><br>7 0 0 0<br>(39) (0) (0) (0   |
| topoiesis 1 2 1 0<br>(11) (22) (11) (0)              | 4 3 1 0<br>(33) (25) (8) (0)  | 4 2 0 0<br>(40)(20)(0)(0)   | 2 3 5 0<br>(11) (17) (28) (0   |
|  |   |   |  |
| <pre>&lt; 9&gt; 0 0 0 0 ( 0) ( 0) ( 0)</pre>         | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <18><br>0 0 1 0<br>( 0) ( 0) ( 6) ( 0  |
| 3  | <pre>     &lt; 9&gt;         0 0 0 0         0         ( 0) ( 0)</pre>  |   |  |

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

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| Organ                        |  | Group Name         0 ppm           No. of Animals on Study         9           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | 3 ppm<br>12<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | 30 ppm<br>18<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|------------------------------|--|--|--|---|---|
| Circulatory s                | system}  |  |  |   | :   |
| heart                        | inflammatory cell nest   | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <18><br>1 0 0 0<br>( 6) ( 0) ( 0) ( 0)            |
|                              | myocardial fibrosis  | 4 0 0 0<br>(44) (0) (0) (0)  | 6 0 0 0<br>(50)(0)(0)(0)                         | 3 1 0 0<br>(30)(10)(0)(0)                             | 9 2 0 0<br>(50) (11) (0) (0)                      |
| rtery/aort                   | arteritis  | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <12><br>0 0 1 0<br>( 0) ( 0) ( 8) ( 0)           | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <18><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
| Digestive sy                 | stem)  |  |  |   |   |
| stomach                      | mineralization   | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <10><br>0 2 0 0<br>( 0) ( 20) ( 0) ( 0)               | <18><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
|                              | inflammatory infiltration  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 1 0 0<br>( 0) ( 8) ( 0) ( 0)                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|                              | erosion:forestomach  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 0 1 0 0<br>( 0) ( 10) ( 0) ( 0)                       | 1 0 0 0<br>(6)(0)(0)(0)                           |
| Grade<br>( a ><br>b<br>( c ) | 1 : Slight 2 : Moderate 3<br>a : Number of animals examined at the s<br>b : Number of animals with lesion<br>c : b / a * 100 | : Marked 4 : Severe<br>ite   |  |   |   |

(HPT150)

| STUDY NO.   | : | 0342           |
|-------------|---|----------------|
| 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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|               |                           |                 |  |  | 10 ppm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |   |  |
|---------------|---------------------------|-----------------|--|--|---|---|--|
| Organ         | Findings                  |                 | 0 ppm<br>dy 9<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 3 ppm<br>12<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |   | 30 ppm<br>18<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |  |
|               |                           | (%) (%          |  |  |   |   |  |
| Digestive sys | stem)                     |                 |  |  |   |   |  |
| stomach       | ulcer:forestomach         | 0 0             | < 9><br>) 0 0<br>)) ( 0) ( 0)                      | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <10><br>0 1 0 0<br>( 0) ( 10) ( 0) ( 0)           | <18><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |  |
|               | hyperplasia:forestomach   | 0 (<br>( 0) ( ( | ) 0 0<br>)) ( 0) ( 0)                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 0 2 0 0<br>( 0) ( 20) ( 0) ( 0)                   | 1 1 0 0<br>(6)(6)(0)(0)                           |  |
|               | erosion:glandular stomach |                 | ) 0 0<br>))(0)(0)                                  | 1 1 0 0<br>(8)(8)(0)(0)                          | 1 0 0 0<br>(10)(0)(0)(0)(0)                       | 1 0 0 0<br>(6)(0)(0)(0)                           |  |
| small intes   | erosion                   | 0 (             | < 9><br>0 0 0<br>0) ( 0) ( 0)                      | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)           | <18><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |  |
| liver         | herniation                | 1 (             | < 9><br>0 0 0<br>0) ( 0) ( 0)                      | <12><br>1 0 0 0<br>( 8) ( 0) ( 0) ( 0)           | <10><br>5 0 0 0<br>(50) (0) (0) (0)               | <18><br>1 0 0 0<br>( 6) ( 0) ( 0) ( 0)            |  |
|               | peliosis-like lesion      |                 | 0 0 0<br>0)(0)(0)                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 1 0 0 0<br>(10) (0) (0) (0)                       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |  |
|               | necrosis:central          |                 | 1 0 0<br>1)(0)(0)                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 3 0 0 0<br>(17) (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

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

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

|              |                              |  | · · · · · · · · · · · · · · · · · · ·   |   | TAGE ·  |
|--------------|------------------------------|--|---|---|---|
| Organ        | Findings                     | Group Name         0 ppm           No. of Animals on Study         9           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $\begin{array}{c} 3 \text{ ppm} \\ 12 \\ \underline{1  2  3  4} \\ \hline (\%)  (\%)  (\%)  (\%) \end{array}$ | 10 ppm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>18<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| {Digestive s | ystem)                       |  |   |   |   |
| liver        | necrosis:focal               | < 9><br>1 0 0 0<br>(11) (0) (0) (0)  | <12><br>2 0 0 0<br>( 17) ( 0) ( 0) ( 0)   | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)           | <18><br>2 0 0 0<br>( 11) ( 0) ( 0) ( 0)           |
|              | fatty change                 | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(8)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 1 0 0 0<br>(6)(0)(0)(0)                           |
|              | granulation                  | 3 0 0 0<br>(33)(0)(0)(0)   | 1 0 0 0<br>(8)(0)(0)(0)   | 1 0 0 0<br>(10) (0) (0) (0)                       | 1 0 0 0<br>(6)(0)(0)(0)                           |
|              | extramedullary hematopoiesis | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 2 0 0 0<br>(11) (0) (0) (0)                       |
|              | acidophilic cell focus       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>(10)(0)(0)(0)                          | 1 0 0 0<br>(6)(0)(0)(0)                           |
|              | basophilic cell focus        | 2 0 0 0<br>(22) (0) (0) (0)  | 5 0 0 0<br>(42)(0)(0)(0)  | 4 0 0 0<br>(40)(0)(0)(0)                          | 8 1 0 0<br>(44)(6)(0)(0)                          |
|              | bile duct hyperplasia        | 3 0 0 0<br>(33)(0)(0)(0)   | 5 0 0 0<br>(42)(0)(0)(0)  | 4 0 0 0<br>(40)(0)(0)(0)                          | 7 0 0 0<br>(39)(0)(0)(0)                          |
| pancreas     | atrophy                      | < 9> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)   | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <18><br>1 0 0 0<br>( 6) ( 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 : 24

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

| SEX         | : FEMALE                               |  |  |  | PAGE : 28   |
|-------------|--|--|--|--|---|
| Organ       | 1                                      | Group Name         0 ppm           No. of Animals on Study         9           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $\begin{array}{c} 3 \text{ ppm} \\ 12 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 10 \text{ ppm} \\ 10 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | 30 ppm<br>18<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| {Urinary sy | vstem)                                 |  |  |  |   |
| kidney      | hyaline droplet                        | <pre> &lt;9&gt; 8 0 0 0 (89) (0) (0) (0) </pre>  | <12><br>11 0 0 0<br>(92) ( 0) ( 0) ( 0)  | <10><br>7 0 0 0<br>(70) ( 0) ( 0) ( 0)   | <18><br>16 0 0 0<br>(89) (0) (0) (0)              |
|             | inflammatory infiltration              | 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) ( 6) ( 0) ( 0)                    |
|             | chronic nephropathy                    | 2 0 0 0<br>(22)(0)(0)(0)   | 3 0 1 0<br>(25)(0)(8)(0)   | 4 0 1 0<br>(40)(0)(10)(0)  | 9 2 0 0<br>(50) (11) (0) (0)                      |
|             | hydronephrosis                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 1 0 0<br>( 0) ( 10) ( 0) ( 0)  | 1 0 0 0<br>(6)(0)(0)(0)                           |
|             | papillary necrosis                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(6)(0)(0)(0)                           |
|             | mineralization:cortico-medullary junct | ion 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 2 0 0 0<br>(20) (0) (0) (0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|             | mineralization:pelvis                  | 2 0 0 0<br>(22)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(10) (0) (0) (0)  | 0 0 0 0<br>(0)(0)(0)(0)                           |
|             | mineralization:cortex                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(10) (0) (0) (0)  | 1 1 0 0<br>(6)(6)(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) DEAD AND MORIBUND ANIMALS (0-105W)

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| )rgan         | 1                                       | Group Name<br>No. of Animals on Stud<br>Grade | 1            | 9<br>2             | ppm<br><u>3</u><br>(%) | <u>4</u><br>(%) |   | 1 (%)      | 12<br>2<br>(%) | 3 ppm<br>2<br>3<br>(%) | <u>4</u><br>(%) | 1(%)      | 2(%      |                         | 3         | 4 (%)   | <u>    1</u><br>(% | ) ( | 18<br>2           | ppm<br><u>3</u><br>(%) | <u>4</u><br>(%) |
|---------------|---|---|--------------|--------------------|------------------------|-----------------|---|------------|----------------|------------------------|-----------------|-----------|----------|-------------------------|-----------|---------|--------------------|-----|-------------------|------------------------|-----------------|
| Jrinary syste | em)                                     |   |              |                    |                        |                 |   |            |                |                        |                 |           |          |                         |           |         |                    |     |                   |                        |                 |
| i dney        | atypical tubule hyperplasia             | . (   | 0<br>0) (    | < 9><br>0<br>0) (  | 0                      | 0               | ( | 0<br>0) (  | <12<br>0<br>0) | 2><br>0<br>( 0) (      | 0<br>0)         | 0<br>( 0) | 0        | <10><br>) (<br>)) ( (   |           | 0<br>0) | 0<br>( 0)          |     | <18><br>1<br>6) ( | ><br>0<br>0)           | 0<br>( 0)       |
| rin bladd     | simple hyperplasia:transitional epithel |   | 0<br>0) (    | < 9><br>1<br>11) ( | 0                      | 0<br>( 0)       | ( | 0<br>0) (  | <12<br>0<br>0) | 2><br>0<br>( 0) (      | 0<br>0)         | 0<br>( 0) | 0        | <10><br>(<br>) (<br>) ( | )<br>)) ( | 0<br>0) | 0<br>( 0)          |     | <18><br>1<br>6) ( | ><br>0<br>0) (         | 0<br>( 0)       |
| indocrine sys | stem}                                   |   |              |                    |                        |                 |   |            |                |                        |                 |           |          |                         |           |         |                    |     |                   |                        |                 |
| tuitary       | angiectasis                             | (   | 0<br>0) (    |                    | 0<br>0) (              | 0<br>( 0)       | ( | 0<br>0) (  | <12<br>0<br>0) | \$><br>0<br>( 0) (     | 0<br>0)         | 0<br>( 0) | 1        | <10><br>(               | )<br>)) ( | 0<br>0) | 4<br>(22)          |     | <18><br>0<br>0) ( | ><br>0<br>0) (         | 0<br>( 0)       |
|               | cyst                                    | (   | 1<br>11) ( 1 |                    | 0<br>0) (              | 0<br>0)         | ( | 3<br>25) ( | 0<br>0) (      | 0<br>( 0) (            | 0<br>0)         | 3<br>(30) | 2<br>(20 | ) ( C                   | )<br>)) ( | 0<br>0) | 4<br>(22)          |     | 9<br>50) (        | 0<br>0) (              | 0<br>( 0)       |
|               | hyperplasia                             | (   | 0<br>0) ( 1  | 1<br>11) (         | 0<br>0) (              | 0<br>0)         | ( | 0<br>0) (  | 0<br>0) (      | 0<br>( 0) (            | 0<br>0)         | 0<br>( 0) | 0<br>( 0 | ) ( 0                   |           | 0<br>0) | 0<br>( 0)          |     | 2<br>1) (         | 0<br>0) (              | 0<br>( 0)       |
|               | Rathke pouch                            | (   | 1<br>11) (   |                    | 0<br>0) (              | 0<br>0)         | ( | 0<br>0) (  | 0<br>0) (      | 0<br>( 0) (            | 0<br>0)         | 0<br>( 0) | 0        | ) ( 0                   | )<br>)) ( | 0<br>0) | 0<br>( 0)          |     | 0<br>0) (         | 0<br>0) (              | 0<br>0)         |

a : Number of animals examined at the site b

b : Number of animals with lesion 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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| rgan       | Findings                          | Group Name         0 ppm           No. of Animals on Study         9           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | 3 ppm<br>12<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>18<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|------------|-----------------------------------|--|--|---|---|
| ndocrine s | ystem)                            |  |  |   |   |
| tuitary    | focal hypertrophy                 | < 9><br>1 0 0 0<br>( 11) ( 0) ( 0) ( 0)  | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <18><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
| yroid      | ultimibranchial body remanet      | <pre>&lt; 9&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>  | <12><br>1 0 0 0<br>( 8) ( 0) ( 0) ( 0)           | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <18><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
|            | C-cell hyperplasia                | 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)                    | 3 0 0 0<br>(17)(0)(0)(0)                          |
|            | focal follicular cell hyperplasia | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 1 0 0 0<br>(6)(0)(0)(0)                           |
| renal      | hemorrhage                        | <pre></pre>  | <12><br>0 1 1 0<br>( 0) ( 8) ( 8) ( 0)           | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <18><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
|            | peliosis-like lesion              | $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 4 3 0 0<br>(33)(25)(0)(0)                        | 1 1 0 0<br>(10) (10) (0) (0)                      | 6 1 0 0<br>(33)(6)(0)(0)                          |
|            | hyperplasia:cortical cell         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 0 0 0 0<br>(0)(0)(0)(0)                           | 0 2 0 0<br>( 0) ( 11) ( 0) ( 0)                   |

(c) c:b/a\*100

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

PAGE : 27

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

| SEX :         | FEMALE                         |  |  |   | PAGE : 28   |
|---------------|--------------------------------|--|--|---|---|
| Organ         | Findings                       | Group Name         0 ppm           No. of Animals on Study         9           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | 3 ppm<br>12<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | 30 ppm<br>18<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| {Endocrine sy | stem}                          |  |  |   |   |
| adrenal       | hyperplasia:medulla            | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <12><br>1 0 0 0<br>( 8) ( 0) ( 0) ( 0)           | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <18><br>0 1 0 0<br>( 0) ( 6) ( 0) ( 0)            |
|               | focal fatty change:cortex      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>(0)(0)(0)(0)                          | 2 3 0 0 *<br>(20)(30)(0)(0)                           | 2 5 1 0<br>(11)(28)(6)(0)                         |
| {Reproductive | system}                        |  |  |   |   |
| ovary         | cyst                           | <pre> &lt; 9&gt;     0 0 0     ( 0) ( 0) ( 0) </pre>   | <12><br>1 0 0 0<br>( 8) ( 0) ( 0) ( 0)           | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <18><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
| uterus        | hemorrhage                     | <pre>&lt; 9&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>  | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <18><br>0 0 1 0<br>( 0) ( 0) ( 6) ( 0)            |
|               | cystic endometrial hyperplasia | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 1 0 0<br>(0)(8)(0)(0)                          | 1 0 0 0<br>(10) (0) (0) (0)                           | 0 1 0 0<br>( 0) ( 6) ( 0) ( 0)                    |
| mammary gl    | galactocele                    | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <12><br>1 0 0 0<br>( 8) ( 0) ( 0) ( 0)           | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <18><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

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

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|             |                           | Group Name 0 ppm<br>No. of Animals on Study 9<br>Grade 1 2 3 4 | 3 ppm<br>12  | 10 ppm<br>10   | 30 ppm<br>18   |
|-------------|---------------------------|--|--|--|--|
| rgan        | Findings                  | Grade <u>1 2 3 4</u><br>(%) (%) (%) (%)                        | $\frac{1}{(\%)} \begin{array}{c} 3 & 4 \\ (\%) & (\%) & (\%) \\ (\%) & (\%) \end{array}$ | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$ | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$ |
| ervous syst | cem)                      |  |  |  |  |
| rain        | hemorrhage                | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                         | <12><br>1 0 0 0<br>( 8) ( 0) ( 0) ( 0)   | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                           | <18><br>1 0 0 0<br>( 6) ( 0) ( 0) ( 0)                           |
|             | inflammatory infiltration | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                 | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | 1 0 0 0<br>(6)(0)(0)(0)  |
|             | gliosis                   | 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)(6)(0)(0)  |
| pecial sens | se organs/appendage)      |  |  |  |  |
| e           | retinal atrophy           | < 9><br>3 0 0 0<br>( 33) ( 0) ( 0) ( 0)                        | <12><br>4 0 0 0<br>( 33) ( 0) ( 0) ( 0)  | <10><br>7 0 0 0<br>( 70) ( 0) ( 0) ( 0)                          | <18><br>14 0 0 0<br>(78) (0) (0) (0)                             |
| arder gl    | degeneration              | < 9><br>1 0 0 0<br>(11) (0) (0) (0)                            | <12><br>1 0 0 0<br>( 8) ( 0) ( 0) ( 0)   | <10><br>1 1 0 0<br>( 10) ( 10) ( 0) ( 0)                         | <18><br>2 0 0 0<br>( 11) ( 0) ( 0) ( 0)                          |
| solacr d    | inflammation              | < 9><br>3 2 0 0<br>( 33) ( 22) ( 0) ( 0)                       | <12><br>4 2 0 0<br>( 33) ( 17) ( 0) ( 0)   | <10><br>3 0 0 0<br>( 30) ( 0) ( 0) ( 0)                          | <pre> &lt;18&gt;     2 0 0 0 *     (11) ( 0) ( 0) ( 0)</pre>     |

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

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

(HPT150)

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

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

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| Organ                  | Ν  | Froup Name<br>No. of Animals on Study<br>Grade <u>1</u> (%) | 0 ppm<br>9<br><u>2 3 4</u><br>(%) (%) (%) | 3 ppm<br>12<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>10<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>18<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|------------------------|--|---|---|--|---|---|
| Musculoskel            | etal system)   |   |   |  |   |   |
| ne                     | osteosclerosis   | 0<br>( 0) (   | < 9><br>0 0 0<br>0) ( 0) ( 0)             | <12><br>1 0 0 0<br>( 8) ( 0) ( 0) ( 0)           | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <18><br>2 2 0 0<br>(11) (11) (0) (0)              |
| ticulus                | arthritis  | 0<br>( 0) (   | < 9><br>0 0 0<br>0) ( 0) ( 0)             | <12><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <10><br>0 1 0 0<br>( 0) ( 10) ( 0) ( 0)           | <18><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
| cade<br>a ><br>b<br>c) | 1 : Slight 2 : Moderate 3 :<br>a : Number of animals examined at the sit<br>b : Number of animals with lesion<br>c : b / a * 100<br>difference ; * : P ≤ 0.05 ** : P ≤ |   |   |  |   |   |

BAIS3

APPENDIX J 6

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

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

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| SEX :          | FEMALE                               |   |  |   | PAGE : 16   |
|----------------|--------------------------------------|---|--|---|---|
| Organ          | Findings                             | Group Name         0 ppm           No. of Animals on Study         41           Grade         1         2         3         4           (%)         (%)         (%)         (%) | $ \begin{array}{c} 3 \text{ ppm} \\ 38 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array} $ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | 30 ppm<br>32<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| {Integumentary | 7 system/appandage)                  |   |  |   |   |
| skin/app       | hyperplasia:epidermis                | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <39><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                | <32><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)            |
|                | scab                                 | 0 0 0 0 0 ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 1 0 0 0<br>(3)(0)(0)(0)                           |
| {Respiratory   | system}                              |   |  |   |   |
| nasal cavit    | thrombus .                           | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <39><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                | <32><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
|                | mineralization                       | 37 0 0 0<br>(90)(0)(0)(0)   | 7 0 0 0 **<br>(18) (0) (0) (0)   | 13 0 0 0 **<br>(33) (0) (0) (0)                       | 27 0 0 0<br>(84) (0) (0) (0)                      |
|                | squamous cell hyperplasia            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 1 0 0 0<br>(3)(0)(0)(0)                           |
|                | goblet cell hyperplasia              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>(3)(0)(0)(0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|                | eosinophilic change:olfactory epithe | elium 6 26 9 0<br>(15) (63) (22) (0)  | 0 10 28 0 **<br>( 0) ( 26) ( 74) ( 0)  | 1 20 18 0 <b>*</b><br>(3) (51) (46) (0)               | 3 27 2 0<br>(9)(84)(6)(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

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

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| )rgan       | Group<br>No. o<br>Grade                     | f Animals on Study | 0 pp<br>41<br><u>2 3</u><br>(%) (% | 4              | 3 pp<br>38<br><u>1 2 3</u><br>(%) (%) (% | 4              | <br>(%)       | 10 ppm<br>39<br>2 3<br>(%) (%) | <u>4</u><br>(%) | <u>1</u><br>(%) (( | 30 ppm<br>32<br>2 <u>3</u><br>%) (%) | 4<br>(%)    |
|-------------|---|--------------------|------------------------------------|----------------|--|----------------|---------------|--------------------------------|-----------------|--------------------|--------------------------------------|-------------|
| Respiratory | system)                                     |                    |                                    |                |  |                |               |                                |                 |                    |                                      |             |
| nasal cavit | eosinophilic change:respiratory epithelium  | 31<br>(76)         | <41><br>6 (<br>(15) ( (            |                | <38><br>32 2 0<br>(84) (5) (0            |                | 32<br>(82) (  | <39><br>1 0<br>3) ( 0)         | 0<br>( 0)       |                    | <32><br>2 0<br>6) ( 0) (             | 0<br>0)     |
|             | inflammation:foreign body                   | 4<br>(10)          | 0 (<br>( 0) ( (                    | ) 0<br>))(0)   | 300<br>(8)(0)(0                          |                | 1<br>( 3) (   | 0 0<br>0) ( 0)                 | 0<br>( 0)       |                    | 0 0<br>0)(0)(                        | 0<br>0)     |
|             | inflammation:respiratory epithelium         | 1<br>( 2)          | 0 (<br>( 0) ( (                    | ) (<br>))( ()  | 0 0 0<br>( 0) ( 0) ( 0                   |                | 3<br>(8)(     | 0 0<br>0) ( 0)                 | 0<br>( 0)       | 14<br>(44) (       | 30<br>9)(0)(                         | 0 *<br>( 0) |
|             | inflammation:olfactory epithelium           | 0<br>( 0)          | 0 (<br>( 0) ( 1                    | 0 0<br>0) ( 0) | 0 0 (<br>( 0) ( 0) ( (                   | 0 0<br>0)(0)   | 0<br>( 0) (   | 0 0<br>0) ( 0)                 | 0<br>( 0)       |                    | 0 0<br>0) ( 0) (                     | 0<br>( 0)   |
|             | respiratory metaplasia:olfactory epithelium |                    | 0                                  | 0 0<br>0) ( 0) | 0 0 0 (                                  | 0 0<br>0)(0)   | 0<br>( 0) (   | 0 0<br>0) ( 0)                 | 0               |                    | 0 0<br>0) ( 0) (                     | 0<br>( 0)   |
|             | respiratory metaplasia:gland                | 41<br>(100)        | 0(0)(                              | 0 0<br>0)(0)   | 37 0 (<br>(97) ( 0) ( 9                  | 00<br>0)(0)    | 39<br>(100) ( | 0 0<br>0) ( 0)                 | 0<br>( 0)       |                    | 0 0<br>0) ( 0) (                     | 0<br>(0)    |
|             | inflammation:transitional epithelium        | 6<br>(15)          | 1<br>(2)(                          | 000)<br>0)(0)  | 13 0<br>(34) (0) (                       | 000)<br>0)(0)  | 13<br>(33) (  | 0 0<br>0) ( 0)                 | 0<br>( 0)       | 7<br>(22) (        | 0 0<br>0)(0)(                        | 0<br>( 0)   |
|             | squamous cell metaplasia;respiratory epith  |                    | 0<br>( 0) (                        | 0 0<br>0) ( 0) | 0 0 (                                    | 0 0<br>0) ( 0) | 2<br>(5)(     | 0 0<br>0) ( 0)                 | 0<br>( 0)       | 4<br>(13) (        | 0 0<br>0) ( 0) (                     | 0<br>( 0)   |

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

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

b b : Number of animals with lesion

(c) c:b/a\*100

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

PAGE : 17

| SEX :        | FEMALE  |   |  |   | PAGE : 1  |
|--------------|---|---|--|---|---|
| Organ        | Group Name<br>No. of Animals on S<br>Grade                      | 0 ppm<br>tudy 41<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 3 ppm<br>38<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>39<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>32<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| {Respiratory | system)   |   |  |   |   |
| nasal cavit  | squamous cell metaplasia with atypia:respiratory epithel<br>ium | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <39><br>1 0 0 0<br>(3) (0) (0) (0)                | <32><br>5 16 0 0 **<br>( 16) ( 50) ( 0) ( 0)      |
|              | squamous cell hyperplasia with atypia                           | 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)                    | 6 1 0 0 **<br>(19) (3) (0) (0)                    |
|              | hyperplasia with atypia:nasal gland                             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 1 0 0 0<br>(3)(0)(0)(0)                           |
|              | hyperplasia with atypia:transitional epithelium                 | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 2 0 0 0<br>(6)(0)(0)(0)                           |
|              | hyperplasia:transitional epithelium                             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 2 0 0 0<br>(5)(0)(0)(0)                          | 7 0 0 0 *<br>(18) (0) (0) (0)                     | 12 2 0 0 **<br>(38) (6) (0) (0)                   |
|              | atrophy:olfactory epithelium                                    | 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)                    | 4 0 0 0<br>(13) (0) (0) (0)                       |
|              | thickening of bone:turbinate                                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 15 0 0 0 ***<br>(38) (0) (0) (0)                  | 14 15 0 0 **<br>(44) (47) (0) (0)                 |
| larynx       | inflammation  | <41><br>13 0 0 0<br>(32) (0) (0) (0)                  | <38><br>11 0 0 0<br>(29) (0) (0) (0)             | <39><br>13 1 0 0<br>(33) (3) (0) (0)              | <32><br>8 0 0 0<br>(25) (0) (0) (0)               |

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

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. : 0342

| REPORT TYPE : | RAT F344/DuCrj<br>A1<br>FEMALE        | SACRIFICED ANIMALS (105W)   | N-NEOPLASTIC LESIONS (SUMMARY)                   |   | PAGE :  |
|---------------|---------------------------------------|---|--|---|---|
| rgan          | Findings                              | Group Name         0 ppm           No. of Animals on Study         41           Grade         1         2         3         4           (%)         (%)         (%)         (%) | 3 ppm<br>38<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>39<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>32<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| Respiratory : | system}                               |   |  |   |   |
| ung           | foreign body granuloma                | <41><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)  | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <39><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <32><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
|               | accumulation of foamy cells           | 2 0 0 0<br>(5)(0)(0)(0)   | 5 0 0 0<br>(13) (0) (0) (0)                      | 1 0 0 0<br>(3)(0)(0)(0)                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|               | bronchiolar-alveolar cell hyperplasia | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 2 1 0 0<br>(5)(3)(0)(0)                           | 1 2 0 0<br>(3)(6)(0)(0)                           |
| Hematopoieti  | c system)                             |   |  |   |   |
| one marrow    | granulation                           | <41><br>7 2 0 0<br>(17) (5) (0) (0)   | <38><br>5 2 0 0<br>(13) (5) (0) (0)              | <39><br>4 3 0 0<br>(10) (8) (0) (0)               | <32><br>5 0 0 0<br>(16) (0) (0) (0)               |
|               | increased hematopoiesis               | 3 1 0 0<br>(7)(2)(0)(0)   | 2 0 0 0<br>(5)(0)(0)(0)                          | 2 0 0 0<br>(5)(0)(0)(0)                           | 5 0 0 0<br>(16)(0)(0)(0)                          |
|               | erythropoiesis:increased              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>(3)(0)(0)(0)                          | 1 0 0 0<br>(3)(0)(0)(0)                           | 1 0 0 0<br>(3)(0)(0)(0)                           |
| hymus         | cyst                                  | <pre>&lt;41&gt; 2 0 0 0 ( 5) ( 0) ( 0) ( 0)</pre>   | <38><br>3 0 0 0<br>( 8) ( 0) ( 0) ( 0)           | <39><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <32><br>2 0 0 0<br>( 6) ( 0) ( 0) ( 0)            |

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

b b : Number of animals with lesion

(c) с: b / а \* 100

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

|             |                              | Group Name 0 ppm<br>No. of Animals on Study 41        | 3 ppm<br>38                            | 10 ppm<br>39   | 30 ppm<br>32                          |
|-------------|------------------------------|---|--|--|---------------------------------------|
| )rgan       | Findings                     | Grade <u>1 2 3 4</u><br>(%) (%) (%) (%)               | <u>1</u> 2 3 4<br>(%) (%) (%) (%)      | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$ | <u>1 2 3 4</u><br>(%) (%) (%) (%      |
| Hematopoie  | ctic system)                 |   |  |  |                                       |
| spleen      | deposit of hemosiderin       | <41><br>35 0 0 0<br>(85) (0) (0) (0)                  | <38><br>33 0 0 0<br>(87) (0) (0) (0)   | <39><br>35 0 0 0<br>(90) (0) (0) (0)                             | <32><br>21 0 0 0<br>(66) (0) (0) (0   |
|             | fibrosis                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0         |
|             | extramedullary hematopoiesis | 29 7 0 0<br>(71)(17)(0)(0)                            | 30 4 0 0<br>(79)(11)(0)(0)             | 33 4 0 0<br>(85)(10)(0)(0)                                       | 22 4 1 0<br>(69)(13)(3)(0             |
| {Circulator | ry system)                   |   |  |  |                                       |
| leart       | thrombus                     | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <39><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                           | <32><br>1 0 0 0<br>( 3) ( 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>(3)(0)(0)(0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0         |
|             | inflammatory cell nest       | $ \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         |
|             | myocardial fibrosis          | 16 3 0 0<br>(39)(7)(0)(0)                             | 20 1 0 0<br>(53) (3) (0) (0)           | 25 0 0 0 *<br>(64) (0) (0) (0)                                   | 17 0 0 0<br>(53)(0)(0)(0              |

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| STUDY NO.   | : | 0342           |
|-------------|---|----------------|
| ANIMAL      | : | RAT F344/DuCrj |
| REPORT TYPE | : | A1             |
| SEX         | : | FEMALE         |

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

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| SEX        | : FEMALE                      |                                                                                                                                                                                             |                                                                                                        |                                                   | PAGE : 21                                                                                                       |
|------------|-------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|---------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|
| Organ      | Findings                      | Group Name         0 ppm           No. of Animals on Study         41           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $\begin{array}{c} 3 \text{ ppm} \\ 38 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array}$ | 10 ppm<br>39<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 30 \text{ ppm} \\ 32 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ |
| {Digestive | system)                       |                                                                                                                                                                                             |                                                                                                        |                                                   |                                                                                                                 |
| tooth      | inflammation                  | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                      | <38><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                                                                 | <39><br>2 0 0 0<br>(5) (0) (0) (0)                | <32><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                          |
| tongue     | arteritis                     | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                      | <38><br>5 0 0 0<br>(13) (0) (0) (0)                                                                    | <39><br>4 0 0 0<br>(10) (0) (0) (0)               | <32><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                                                                          |
| stomach    | inflammatory infiltration     | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                      | <38><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                                                                 | <39><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <32><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                          |
|            | erosion:glandular stomach     | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                                                                                       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 1 0 0 0<br>(3)(0)(0)(0)                                                                                         |
|            | hyperplasia:glandular stomach | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                         | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                  |
| liver      | herniation                    | <41><br>14 0 0 0<br>(34) (0) (0) (0)                                                                                                                                                        | <38><br>3 0 0 0 *<br>( 8) ( 0) ( 0) ( 0)                                                               | <39><br>9 0 0 0<br>(23) (0) (0) (0)               | <32><br>3 0 0 0 *<br>( 9) ( 0) ( 0) ( 0)                                                                        |
|            | peliosis-like lesion          | 2 0 0 0<br>(5)(0)(0)(0)                                                                                                                                                                     | 1 0 0 0<br>(3)(0)(0)(0)                                                                                | 1 0 0 0<br>(3)(0)(0)(0)                           | 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

| SEX         | : FEMALE                  |                                                                                                                                                                                 |                                                                                                                    |                                                   | PAGE :                                            |
|-------------|---------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| )rgan       | Findings                  | Group Name         0 ppm           No. of Animals on Study         41           Grade         1         2         3         4           (%)         (%)         (%)         (%) | $\begin{array}{c} 3 \text{ ppm} \\ 38 \\ \underline{1  2  3  4} \\ \underline{(\%)  (\%)  (\%)  (\%)} \end{array}$ | 10 ppm<br>39<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>32<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|             |                           |                                                                                                                                                                                 |                                                                                                                    |                                                   |                                                   |
| Digestive : | system}                   |                                                                                                                                                                                 |                                                                                                                    |                                                   |                                                   |
| iver        | necrosis:focal            | <41><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                                                                                                          | <38><br>3 1 0 0<br>(8) (3) (0) (0)                                                                                 | <39><br>3 1 0 0<br>( 8) ( 3) ( 0) ( 0)            | <32><br>4 1 0 0<br>(13) (3) (0) (0)               |
|             | fatty change              | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                                                                           | 1 0 0 0<br>(3)(0)(0)(0)                                                                                            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 1 0 0 0<br>(3)(0)(0)(0)                           |
|             | inflammatory infiltration | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                  | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                                                                                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|             | lymphocytic infiltration  | 1 1 0 0<br>(2)(2)(0)(0)                                                                                                                                                         | 2 0 0 0<br>(5)(0)(0)(0)                                                                                            | 2 0 0 0<br>(5)(0)(0)(0)                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|             | granulation               | 25 2 0 0<br>(61)(5)(0)(0)                                                                                                                                                       | 21 6 1 0<br>(55)(16)(3)(0)                                                                                         | 22 4 0 0<br>(56)(10)(0)(0)                        | 11 4 0 0<br>(34) (13) (0) (0)                     |
|             | organization              | 0 1 0 0<br>( 0) ( 2) ( 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)                    |
|             | perivascular inflammation | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                  | 0 0 0 0<br>(0)(0)(0)(0)                                                                                            | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|             | fibrosis:focal            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                     | 0 1 0 0<br>(0)(3)(0)(0)                           | 0 0 0 0<br>(0)(0)(0)(0)                           |

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

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(c)

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

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| SEX          | SEX : FEMALE                 |                                                                                           |                                                       |                                                       |                                                   |
|--------------|------------------------------|-------------------------------------------------------------------------------------------|-------------------------------------------------------|-------------------------------------------------------|---------------------------------------------------|
| Organ        | Findings                     | Group Name 0 ppm<br>No. of Animals on Study 41<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | 30 ppm<br>32<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| {Digestive s | system}                      |                                                                                           |                                                       |                                                       |                                                   |
| liver        | extramedullary hematopoiesis | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                    | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <39><br>2 0 0 0<br>( 5) ( 0) ( 0) ( 0)                | <32><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
|              | clear cell focus             | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                                      | 0 0 0 0<br>(0)(0)(0)(0)(0)                            | 6 1 0 0<br>(15) (3) (0) (0)                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|              | acidophilic cell focus       | 2 2 0 0<br>(5)(5)(0)(0)                                                                   | 2 1 0 0<br>(5)(3)(0)(0)                               | 4 1 0 0<br>(10) (3) (0) (0)                           | 5 1 0 0<br>(16) (3) (0) (0)                       |
|              | basophilic cell focus        | 32 3 0 0<br>(78)(7)(0)(0)                                                                 | 24 9 0 0<br>(63)(24)(0)(0)                            | 29 4 0 0<br>(74) (10) (0) (0)                         | 22 3 0 0<br>(69)(9)(0)(0)                         |
|              | bile duct hyperplasia        | 30 0 0 0<br>(73)(0)(0)(0)                                                                 | 26 1 0 0<br>(68)(3)(0)(0)                             | 32 1 0 0<br>(82) (3) (0) (0)                          | 22 0 0 0<br>(69)(0)(0)(0)                         |
|              | cholangiofibrosis            | 0 0 1 0<br>( 0) ( 0) ( 2) ( 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)                    |
| pancreas     | atrophy                      | $\langle 41 \rangle$<br>1 0 0 0<br>(2) (0) (0) (0)                                        | <38><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                | <39><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <32><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)            |
|              | islet cell hyperplasia       | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                                                            | 1 1 0 0<br>(3)(3)(0)(0)                               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 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

| rgan        | Group<br>No. of<br>Grade                  | Name         0 ppm           'Animals on Study         41 | 3 ppm<br>38<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>39<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>32<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|-------------|-------------------------------------------|-----------------------------------------------------------|--------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| lrinary sys | tem)                                      |                                                           |                                                  |                                                   |                                                   |
| dney.       | infarct                                   | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | <38><br>2 0 0 0<br>(5) (0) (0) (0)               | <39><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)            | <32><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)            |
|             | cyst                                      | 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)                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|             | hyaline droplet                           | 40 0 0 0<br>(98) (0) (0) (0)                              | 37 0 0 0<br>(97)(0)(0)(0)                        | 39 0 0 0<br>(100) ( 0) ( 0) ( 0)                  | 32 0 0 0<br>(100) ( 0) ( 0) ( 0)                  |
|             | chronic nephropathy                       | 30 6 0 0<br>(73)(15)(0)(0)                                | 22 9 5 0 <b>*</b><br>(58) (24) (13) (0)          | 22 10 2 0<br>(56)(26)(5)(0)                       | 19 8 3 0<br>(59)(25)(9)(0)                        |
|             | mineralization:cortico-medullary junction | 1 0 0 0<br>(2)(0)(0)(0)                                   | 2 0 0 0<br>(5)(0)(0)(0)                          | 1 0 0 0<br>(3)(0)(0)(0)                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|             | mineralization:papilla                    | 2 0 0 0<br>(5)(0)(0)(0)                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 1 0 0 0<br>(3)(0)(0)(0)                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|             | mineralization:pelvis                     | 7 0 0 0<br>(17) (0) (0) (0)                               | 2 0 0 0<br>(5)(0)(0)(0)                          | 0 0 0 0 *<br>(0)(0)(0)(0)                         | 2 0 0 0<br>(6)(0)(0)(0)                           |
| Indocrine s | ystem)                                    |                                                           |                                                  |                                                   |                                                   |
| tuitary     | angiectasis                               | <41><br>3 2 0 0<br>( 7) ( 5) ( 0) ( 0)                    | <38><br>7 2 1 0<br>(18) (5) (3) (0)              | <39><br>0 5 1 0<br>( 0) ( 13) ( 3) ( 0)           | <32><br>1 1 0 0<br>( 3) ( 3) ( 0) ( 0)            |

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

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# STUDY NO. : 0342 ANIMAL : RAT F344/DuCri

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

(1100+ = ^)

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

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| Organ       | Findings                          | Group Name         0 ppm           No. of Animals on Study         41           Grade         1         2         3         4           (%)         (%)         (%)         (%) | $\begin{array}{c} 3 \text{ ppm} \\ 38 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array}$ | 10 ppm<br>39<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>32<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|-------------|-----------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| Endocrine s | ystem}                            |                                                                                                                                                                                 |                                                                                                        |                                                   |                                                   |
| ituitary    | cyst                              | <41><br>12 7 2 0<br>(29) (17) (5) (0)                                                                                                                                           | <38><br>16 7 2 0<br>(42) (18) (5) (0)                                                                  | <39><br>15 7 0 0<br>(38) (18) (0) (0)             | <32><br>16 4 2 0<br>(50) (13) (6) (0)             |
|             | hyperplasia                       | 4 3 0 0<br>(10) (7) (0) (0)                                                                                                                                                     | 3 1 0 0<br>(8)(3)(0)(0)                                                                                | 7 7 0 0<br>(18) (18) (0) (0)                      | 4 3 1 0<br>(13) (9) (3) (0)                       |
|             | Rathke pouch                      | 2 0 0 0<br>(5)(0)(0)(0)                                                                                                                                                         | 1 0 0 0<br>(3)(0)(0)(0)                                                                                | 1 0 0 0<br>(3)(0)(0)(0)                           | 2 0 0 0<br>(6)(0)(0)(0)                           |
|             | focal hypertrophy                 | 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>(6)(0)(0)(0)(0)                        |
| nyroid      | ultimibranchial body remanet      | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                          | <38><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                                                                 | <39><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <32><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
|             | C-cell hyperplasia                | 12 1 0 0<br>(29) (2) (0) (0)                                                                                                                                                    | 8 2 0 0<br>(21)(5)(0)(0)                                                                               | 13 0 0 0<br>(33) (0) (0) (0)                      | 6 0 0 0<br>(19)(0)(0)(0)                          |
|             | focal follicular cell hyperplasia | 1 0 0 0<br>(2)(0)(0)(0)                                                                                                                                                         | 1 0 0 0<br>(3)(0)(0)(0)                                                                                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
| drenal      | hemorrhage                        | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                          | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                 | <39><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)            | <32><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

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

| )rgan     | Findings                     | Group Name         0 ppm           No. of Animals on Study         41           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $3 ppm$ $38$ $\frac{1}{(7)} 2 \frac{3}{(7)} 4$ $(7)$ | $ \begin{array}{c} 10 \text{ ppm} \\ 39 \\ \underline{1} & \underline{2} & \underline{3} & \underline{4} \\ (1) & (1) & (2) & (2) \end{array} $ | 30 ppm<br>32<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|-----------|------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|
|           | Fillulings                   | (%) (%) (%) (%)                                                                                                                                                                             | (%) (%) (%) (%)                                      | (%) (%) (%) (%)                                                                                                                                 | (%) (%) (%) (%)                                   |
| Endocrine | system)                      |                                                                                                                                                                                             |                                                      |                                                                                                                                                 |                                                   |
| drenal    | peliosis-like lesion         | <41><br>21 18 0 0<br>(51) (44) (0) (0)                                                                                                                                                      | <38><br>24 8 0 0<br>(63) (21) (0) (0)                | <39><br>28 6 0 0 *<br>(72) (15) (0) (0)                                                                                                         | <32><br>21 5 0 0 *<br>(66) (16) (0) (0)           |
|           | cyst                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                              | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|           | extramedullary hematopoiesis | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       | 1 0 0 0<br>(3)(0)(0)(0)                                                                                                                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|           | hyperplasia:cortical cell    | 1 0 0 0<br>(2)(0)(0)(0)                                                                                                                                                                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       | 0 2 0 0<br>( 0) ( 5) ( 0) ( 0)                                                                                                                  | 1 3 0 0<br>(3)(9)(0)(0)                           |
|           | hyperplasia:medulla          | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                                                                                       | .1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                      | 2 0 0 0<br>(5)(0)(0)(0)                                                                                                                         | 2 0 0 0<br>(6)(0)(0)(0)                           |
|           | focal fatty change:cortex    | 8 2 0 0<br>(20) (5) (0) (0)                                                                                                                                                                 | 12 1 0 0<br>(32) (3) (0) (0)                         | 9 3 0 0<br>(23)(8)(0)(0)                                                                                                                        | 8 5 0 0<br>(25)(16)(0)(0)                         |
| eproducti | ve system)                   |                                                                                                                                                                                             |                                                      |                                                                                                                                                 |                                                   |
| vary      | cyst                         | <41><br>1 1 0 0<br>( 2) ( 2) ( 0) ( 0)                                                                                                                                                      | <38><br>0 2 0 0<br>( 0) ( 5) ( 0) ( 0)               | <39><br>1 2 0 0<br>( 3) ( 5) ( 0) ( 0)                                                                                                          | <32><br>2 0 0 0<br>( 6) ( 0) ( 0) ( 0)            |

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

| SEX          | FEMALE                         |                                                                                                                                                                      |             |                                                                                                        |                                                   | PAGE                                              |
|--------------|--------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------|--------------------------------------------------------------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| )rgan        | Findings                       | Group Name         0 pp           No. of Animals on Study         41           Grade         1         2         3           (%)         (%)         (%)         (%) | 4           | $\begin{array}{c} 3 \text{ ppm} \\ 38 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array}$ | 10 ppm<br>39<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>32<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| Reproductive | e system)                      |                                                                                                                                                                      |             |                                                                                                        |                                                   |                                                   |
| iterus       | dilatation                     | <41><br>0 0 0<br>( 0) ( 0) ( 0)                                                                                                                                      |             | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                 | <39><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)            | <32><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
|              | inflammation                   | 0 0 0<br>( 0) ( 0) ( 0)                                                                                                                                              |             | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                                                                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|              | hyperplasia:epithelium         | $\begin{pmatrix} 1 & 0 & 0 \\ ( & 2) & ( & 0) & ( & 0) \end{pmatrix}$                                                                                                |             | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                                                                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    |
|              | hyperplasia:gland              | 1 0 0<br>(2)(0)(0                                                                                                                                                    | 0<br>) ( 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)                    |
|              | cystic endometrial hyperplasia | 6 2 0<br>(15)(5)(0                                                                                                                                                   | 0<br>) ( 0) | 3 1 0 0<br>(8) (3) (0) (0)                                                                             | 2 0 0 0<br>(5)(0)(0)(0)                           | 2 3 0 0<br>(6)(9)(0)(0)                           |
| agina        | squamous cell hyperplasia      | <41><br>0 0 0<br>( 0) ( 0) ( 0                                                                                                                                       |             | <38><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                                                                 | <39><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <32><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
| ammary gl    | hyperplasia                    | <41><br>1 0 0<br>( 2) ( 0) ( 0                                                                                                                                       |             | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                 | <39><br>0 2 0 0<br>( 0) ( 5) ( 0) ( 0)            | <32><br>0 0 0 0<br>( 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  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

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

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| Organ                    | Findings                                                                                                                 | Group Name         0 ppm           No. of Animals on Study         41           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | 3 ppm<br>38<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>39<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 30 ppm<br>32<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|--------------------------|--------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| {Reproductive            | system)                                                                                                                  |                                                                                                                                                                                             |                                                  |                                                   |                                                   |
| nanmary gl               | galactocele                                                                                                              | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                      | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <39><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <32><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)            |
| {Nervous syst            | em)                                                                                                                      |                                                                                                                                                                                             |                                                  |                                                   |                                                   |
| orain                    | necrosis:focal                                                                                                           | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                      | <38><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <39><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <32><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)            |
|                          | inflammatory infiltration                                                                                                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                    | 0 I 0 0<br>( 0) ( 3) ( 0) ( 0)                    |
|                          | gliosis                                                                                                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                              | 2 0 0 0<br>(5)(0)(0)(0)                          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 0 2 0 0<br>( 0) ( 6) ( 0) ( 0)                    |
| Special sens             | e organs/appendage)                                                                                                      |                                                                                                                                                                                             |                                                  |                                                   |                                                   |
| eye                      | cataract                                                                                                                 | <41><br>0 3 0 0<br>( 0) ( 7) ( 0) ( 0)                                                                                                                                                      | <38><br>0 1 1 0<br>( 0) ( 3) ( 3) ( 0)           | <39><br>0 2 0 0<br>( 0) ( 5) ( 0) ( 0)            | <32><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            |
| Grade<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 | 3 : Marked 4 : Severe<br>site                                                                                                                                                               |                                                  |                                                   |                                                   |

(HPT150)

BAIS3

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

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| SEX :         | FEMALE                   |                                                                                                                                                                                             |                                                  |                                                   | PAGE : 29                                                                                               |
|---------------|--------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------|---------------------------------------------------------------------------------------------------------|
| Organ         | Pindings                 | Group Name         0 ppm           No. of Animals on Study         41           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | 3 ppm<br>38<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10 ppm<br>39<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 30 \text{ ppm} \\ 32 \\ \underline{1  2  3  4} \\ (\%)  (\%)  (\%)  (\%) \end{array}$ |
| {Special sens | se organs/appendage}     |                                                                                                                                                                                             |                                                  |                                                   |                                                                                                         |
| еуе           | retinal atrophy          | <41><br>39 1 1 0<br>(95) (2) (2) (0)                                                                                                                                                        | <38><br>36 0 2 0<br>(95) (0) (5) (0)             | <39><br>37 0 2 0<br>(95) (0) (5) (0)              | <32><br>32 0 0 0<br>(100) ( 0) ( 0) ( 0)                                                                |
|               | keratitis                | 3 0 0 0<br>(7)(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)                                                                          |
|               | iritis                   | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                                                                                                                                                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                          |
| Harder gl     | degeneration             | <41><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                                                                                                                                      | <38><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)           | <39><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)            | <32><br>2 1 0 0<br>( 6) ( 3) ( 0) ( 0)                                                                  |
|               | lymphocytic infiltration | 3 0 0 0<br>(7)(0)(0)(0)                                                                                                                                                                     | 3 0 0 0<br>(8)(0)(0)(0)                          | 4 0 0 0<br>(10) (0) (0) (0)                       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                          |
|               | granulation              | 3 0 0 0<br>(7)(0)(0)(0)                                                                                                                                                                     | 1 0 0 0<br>(3)(0)(0)(0)                          | 1 0 0 0<br>(3)(0)(0)(0)                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                          |
|               | hyperplasia:mast cell    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 1 0 0 0<br>(3)(0)(0)(0)                                                                                 |
| nasolacr d    | inflammation             | <41><br>19 4 0 0<br>(46) (10) (0) (0)                                                                                                                                                       | 9400<br>(24)(11)(0)(0)                           | <39><br>5 0 0 0 **<br>(13) (0) (0) (0)            | `<32><br>2 0 0 0 **<br>( 6) ( 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.<br>ANIMAL<br>REPORT TYP<br>SEX | : 0342<br>: RAT F344/DuCrj<br>E : A1<br>: FEMALE                                                                    | HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)<br>SACRIFICED ANIMALS (105W)          |                                     |                                        |                                     |  |  |  |
|------------------------------------------|---------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|-------------------------------------|----------------------------------------|-------------------------------------|--|--|--|
|                                          |                                                                                                                     |                                                                                               |                                     |                                        | PAGE : 30                           |  |  |  |
|                                          |                                                                                                                     | Group Name 0 ppm<br>No. of Animals on Study 41<br>Grade <u>1 2 3 4</u>                        | 3 ppm<br>38<br>1 2 3 4              | 10 ppm<br>39<br>1 2 3 4                | 30 ppm<br>32<br>1 2 3 4             |  |  |  |
| Organ                                    | _ Findings                                                                                                          | (%) (%) (%)                                                                                   | (%) (%) (%) (%)                     | (%) (%) (%) (%)                        | (%) (%) (%) (%)                     |  |  |  |
| {Musculosk                               | eletal system}                                                                                                      |                                                                                               |                                     |                                        |                                     |  |  |  |
| bone                                     | osteosclerosis                                                                                                      | $\begin{array}{cccc} & <41 \\ 3 & 1 & 1 & 0 \\ ( & 7) & ( & 2) & ( & 2) & ( & 0) \end{array}$ | <38><br>5 0 0 0<br>(13) (0) (0) (0) | <39><br>2 1 0 0<br>( 5) ( 3) ( 0) ( 0) | <32><br>7 0 0 0<br>(22) (0) (0) (0) |  |  |  |
| Grade<br>< a ><br>b<br>( c )             | 1 : Slight 2 : Moderate<br>a : Number of animals examined a<br>b : Number of animals with lesion<br>c : b / a * 100 |                                                                                               |                                     |                                        |                                     |  |  |  |

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(HPT150)

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

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APPENDIX K 1

## 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. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

PAGE: 1

| Time-related<br>Weeks | Items                                          | Group Name | 0 ppm | 3 ppm | 10 ppm | 30 ppm |  |
|-----------------------|------------------------------------------------|------------|-------|-------|--------|--------|--|
| 0 - 52                | NO. OF EXAMINED ANIMALS                        |            | 0     | 0     | 0      | 0      |  |
|                       | NO. OF ANIMALS WITH TUMORS                     |            | 0     | 0     | 0      | 0      |  |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS              |            | 0     | õ     | Õ      | ů      |  |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS            |            | 0     | 0     | 0      | 0      |  |
|                       | NO. OF BENIGN TUMORS                           |            | 0     | 0     | 0      | 0      |  |
|                       | NO. OF MALIGNANT TUMORS                        |            | 0     | 0     | 0      | 0      |  |
|                       | NO. OF TOTAL TUMORS                            |            | 0     | 0     | 0      | 0      |  |
| 53 - 78               | NO. OF EXAMINED ANIMALS                        |            | 1     | 4     | 0      | 4      |  |
| ٠                     | NO. OF ANIMALS WITH TUMORS                     |            | 1     | 3     | 0      | 4      |  |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS              |            | 1     | 2     | 0      | ō      |  |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS            |            | 0     | 1     | 0      | 4      |  |
|                       | NO. OF BENIGN TUMORS                           |            | 0     | 1     | 0      | 6      |  |
|                       | NO. OF MALIGNANT TUMORS                        |            | 1     | 3     | 0      | 4      |  |
|                       | NO. OF TOTAL TUMORS                            |            | 1     | 4     | 0      | 10     |  |
| 79 - 104              | NO. OF EXAMINED ANIMALS                        |            | 9     | 4     | 12     | 23     |  |
|                       | NO. OF ANIMALS WITH TUMORS                     |            | 9     | 4     | 12     | 22     |  |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS              |            | 3     | 0     | 3      | 0      |  |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS            |            | 6     | 4     | 9      | 22     |  |
|                       | NO. OF BENIGN TUMORS                           |            | 12    | 7     | 18     | . 46   |  |
|                       | NO. OF MALIGNANT TUMORS                        |            | 6     | 2     | 13     | 29     |  |
|                       | NO. OF TOTAL TUMORS                            |            | 18    | 9     | 31     | 75     |  |
| 105 - 105             | NO. OF EXAMINED ANIMALS                        |            | 40    | 42    | 38     | 23     |  |
|                       | NO. OF ANIMALS WITH TUMORS                     |            | 39    | 40    | 38     | 23     |  |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS              |            | 11    | 10    | 10     | 1      |  |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS            |            | 28    | 30    | 28     | 22     |  |
|                       | NO. OF BENIGN TUMORS                           |            | 82    | 80    | 80     | 63     |  |
|                       | NO. OF MALIGNANT TUMORS<br>NO. OF TOTAL TUMORS |            | 13    | 7     | 14     | 27     |  |
|                       | NO. OF TOTAL TUMORS                            |            | 95    | 87    | 94     | 90     |  |

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STUDY NO. : 0342 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

PAGE : 2

| ime-related<br>Weeks | Items                               | Group Name | 0 ppm | 3 ppm | 10 ppm | 30 ppm |  |
|----------------------|-------------------------------------|------------|-------|-------|--------|--------|--|
| 0 - 105              | NO. OF EXAMINED ANIMALS             |            | 50    | 50    | 50     | 50     |  |
|                      | NO. OF ANIMALS WITH TUMORS          |            | 49    | 47    | 50     | 49     |  |
|                      | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 15    | 12    | 13     | 1      |  |
|                      | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 34    | 35    | 37     | 48     |  |
|                      | NO. OF BENIGN TUMORS                |            | 94    | 88    | 98     | 115    |  |
|                      | NO. OF MALIGNANT TUMORS             |            | 20    | 12    | 27     | 60     |  |
|                      | NO. OF TOTAL TUMORS                 |            | 114   | 100   | 125    | 175    |  |

(HP1070)

BAIS3

APPENDIX K 2

# NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED, RAT : FEMALE

(2-YEAR STUDY)

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

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PAGE : 3

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| lime-related<br>Weeks | Items                               | Group Name | 0 ppm | 3 ppm | 10 ppm | 30 ppm |  |
|-----------------------|-------------------------------------|------------|-------|-------|--------|--------|--|
| 0 - 52                | NO. OF EXAMINED ANIMALS             |            | 0     | 0     | 0      | 0      |  |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 0     | 0     | 0      | 0      |  |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 0     | 0     | 0      | 0      |  |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0     | 0     | õ      | 0      |  |
|                       | NO. OF BENIGN TUMORS                |            | 0     | 0     | 0      | 0      |  |
|                       | NO. OF MALIGNANT TUMORS             |            | 0     | 0     | 0      | 0      |  |
|                       | NO. OF TOTAL TUMORS                 |            | 0     | 0     | 0      | 0      |  |
| 53 - 78               | NO. OF EXAMINED ANIMALS             |            | 3     | 1     | 2      | 3      |  |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 2     | . 0   | 2      | 2      |  |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 2     | 0     | 2      | 1      |  |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0     | 0     | 0      | 1      |  |
|                       | NO. OF BENIGN TUMORS                |            | 2     | 0     | 0      | 1      |  |
|                       | NO. OF MALIGNANT TUMORS             |            | 0     | 0     | 2      | 2      |  |
|                       | NO. OF TOTAL TUMORS                 |            | 2     | 0     | 2      | 3      |  |
| 79 - 104              | NO. OF EXAMINED ANIMALS             |            | 6     | 11    | 8      | 15     |  |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 5     | 11    | 8      | 15     |  |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 3     | 8     | 2      | 3      |  |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 2     | 3     | 6      | 12     |  |
|                       | NO. OF BENIGN TUMORS                |            | 3     | 8     | 10     | 19     |  |
|                       | NO. OF MALIGNANT TUMORS             |            | 4     | 6     | 9      | 13     |  |
|                       | NO. OF TOTAL TUMORS                 |            | 7     | 14    | 19     | 32     |  |
| 105 - 105             | NO. OF EXAMINED ANIMALS             |            | 41    | 38    | 39     | 32     |  |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 26    | 29    | 31     | 28     |  |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 12    | 16    | 9      | 6      |  |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 14    | 13    | 22     | 22     |  |
|                       | NO. OF BENIGN TUMORS                |            | 41    | 36    | 57     | 52     |  |
|                       | NO. OF MALIGNANT TUMORS             |            | 6     | 10    | 7      | 13     |  |
|                       | NO. OF TOTAL TUMORS                 |            | 47    | 46    | 64     | 65     |  |

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

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PAGE: 4

| Time-related<br>Weeks | Items                                                                    | Group Name | 0 ppm    | 3 ppm    | 10 ppm   | 30 ppm    |    |
|-----------------------|--------------------------------------------------------------------------|------------|----------|----------|----------|-----------|----|
| 0 - 105               | NO. OF EXAMINED ANIMALS                                                  |            | 50       | 50       | 49       | 50        |    |
|                       | NO. OF ANIMALS WITH TUMORS                                               |            | 33       | 40       | 41       | 45        |    |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS<br>NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 17<br>16 | 24<br>16 | 13<br>28 | 10<br>35  |    |
|                       | NO. OF BENIGN TUMORS                                                     |            | 46       | 44       | 67       | 72        |    |
|                       | NO. OF MALIGNANT TUMORS<br>NO. OF TOTAL TUMORS                           |            | 10<br>56 | 16<br>60 | 18<br>85 | 28<br>100 |    |
| (HPT070)              |                                                                          |            |          |          |          |           | DA |

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APPENDIX L 1

### HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS : SUMMARY

RAT : MALE

(2-YEAR STUDY)

|               | : 0342<br>: RAT F344/DuCrj<br>: A1 | HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)<br>ALL ANIMALS (0-105W) |                  |                 |                   |                 |  |  |  |  |
|---------------|------------------------------------|------------------------------------------------------------------------------|------------------|-----------------|-------------------|-----------------|--|--|--|--|
| SEX :         | : MALE                             |                                                                              |                  | ·····           |                   | PAGE :          |  |  |  |  |
| Organ         | Findings                           | Group Name<br>No. of animals on Study                                        | 0 ppm<br>50      | 3 ppm<br>50     | 10 ppm<br>50      | 30 ppm<br>50    |  |  |  |  |
| {Integumentar | ry system/appandage}               |                                                                              |                  |                 |                   |                 |  |  |  |  |
| skin/app      | squamous cell papilloma            |                                                                              | <50><br>0 ( 0%)  | <50><br>0 ( 0%) | <50><br>1 ( 2%)   | <50><br>3 ( 6%) |  |  |  |  |
|               | trichoepithelioma                  |                                                                              | 0 ( 0%)          | 1 ( 2%)         | 1 ( 2%)           | 1 ( 2%)         |  |  |  |  |
|               | keratoacanthoma                    |                                                                              | 3 ( 6%)          | 3 ( 6%)         | 0 ( 0%)           | 2 ( 4%)         |  |  |  |  |
|               | sebaceous adenoma                  |                                                                              | 0 ( 0%)          | 0 ( 0%)         | 0 ( 0%)           | 1 ( 2%)         |  |  |  |  |
| subcutis      | fibroma                            |                                                                              | <50><br>10 (20%) | <50><br>2 ( 4%) | <50><br>10 ( 20%) | <50><br>9 (18%) |  |  |  |  |
|               | lipoma                             |                                                                              | 0 ( 0%)          | 1 ( 2%)         | 1 ( 2%)           | 0 ( 0%)         |  |  |  |  |
|               | schwannoma                         |                                                                              | 2 ( 4%)          | 1 ( 2%)         | 0 ( 0%)           | 0 ( 0%)         |  |  |  |  |
|               | fibrosarcoma                       |                                                                              | 0 ( 0%)          | 0 ( 0%)         | 1 ( 2%)           | 1 ( 2%)         |  |  |  |  |
|               | schwannoma:malignant               |                                                                              | 0 ( 0%)          | 0 ( 0%)         | 0 ( 0%)           | 1 ( 2%)         |  |  |  |  |
| {Respiratory  | system)                            |                                                                              |                  |                 |                   |                 |  |  |  |  |
| nasal cavit   | adenoma                            |                                                                              | <50><br>0 ( 0%)  | <50><br>0 ( 0%) | <50><br>3 ( 6%)   | <50><br>5 (10%) |  |  |  |  |
|               | squamous cell carcinoma            |                                                                              | 0 ( 0%)          | 0 ( 0%)         | 0 ( 0%)           | 14 (28%)        |  |  |  |  |
|               | adenocarcinoma                     |                                                                              | 0 ( 0%)          | 0 ( 0%)         | 0 ( 0%)           | 1 ( 2%)         |  |  |  |  |
|               |                                    |                                                                              | ·                |                 |                   |                 |  |  |  |  |

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

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

(HPT085)

BAIS3

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

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| Organ          | Findings                       | Group Name<br> |   | 0 ppm<br>50   |   | 3 ppm<br>50     |   | 10 ppm<br>50   |   | 30 ppm<br>50  |  |
|----------------|--------------------------------|----------------|---|---------------|---|-----------------|---|----------------|---|---------------|--|
| {Respiratory : | system}                        |                |   |               |   |                 |   |                |   |               |  |
| nasal cavit    | basal cell carcinoma           |                | 0 | <50><br>( 0%) | C | <50><br>( 0%)   | 0 | <50><br>( 0%)  | 1 | <50><br>( 2%) |  |
| lung           | bronchiolar-alveolar adenoma   |                | 2 | <50><br>( 4%) | 4 | <50><br>( 8%)   | 5 | <50><br>( 10%) | 3 | <50><br>( 6%) |  |
|                | bronchiolar-alveolar carcinoma |                | 4 | ( 8%)         | 3 | 3 ( 6%)         | 2 | ( 4%)          | 0 | ( 0%)         |  |
| {Hematopoieti  | c system)                      |                |   |               |   |                 |   |                |   |               |  |
| lymph node     | malignant lymphoma             |                | 0 | <50><br>( 0%) | C | <50><br>) ( 0%) | 1 | <50><br>( 2%)  | 0 | <50><br>( 0%) |  |
| spleen         | histiocytic sarcoma            |                | 1 | <50><br>( 2%) | C | <50><br>) ( 0%) | 0 | <50><br>( 0%)  | 0 | <50><br>( 0%) |  |
|                | mononuclear cell leukemia      |                | 8 | (16%)         | 1 | L (2%)          | 4 | ( 8%)          | 5 | ( 10%)        |  |
| {Digestive sy  | stem)                          |                |   |               |   |                 |   |                |   |               |  |
| oral cavity    | squamous cell carcinoma        |                | 0 | <50><br>( 0%) | ( | <50><br>0 ( 0%) | 1 | <50><br>( 2%)  | 0 | <50><br>( 0%) |  |
| salivary gl    | fibroma                        |                | 0 | <50><br>( 0%) | ¢ | <50><br>D ( 0%) | 1 | <50><br>(2%)   | 0 | <50><br>( 0%) |  |
|                | adenocarcinoma                 |                | 0 | ( 0%)         | : | 1 (2%)          | C | ( 0%)          | 0 | ( 0%)         |  |
| stomach        | squamous cell papilloma        |                | 0 | <50><br>( 0%) |   | <50><br>1 ( 2%) | C | <50><br>(0%)   | 0 | <50><br>( 0%) |  |
| small intes    | adenocarcinoma                 |                | 0 | <50><br>( 0%) |   | <50><br>0 ( 0%) | ( | <50><br>( 0%)  | 1 | <50><br>( 2%) |  |
|                |                                |                |   |               |   |                 |   |                |   |               |  |

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

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

PAGE: 2

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

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| SEX :          | MALE                           |                                       |    |                |    |                |    |                  |    | PAGE :         | 3 |
|----------------|--------------------------------|---------------------------------------|----|----------------|----|----------------|----|------------------|----|----------------|---|
| Organ          | Findings                       | Group Name<br>No. of animals on Study |    | 0 ppm<br>50    |    | 3 ppm<br>50    |    | 10 ppm<br>50     |    | 30 ppm<br>50   |   |
| {Digestive sys | stem)                          |                                       |    |                |    |                |    |                  |    |                |   |
| small intes    | malignant fibrous histiocytoma |                                       | 0  | <50><br>( 0%)  | 0  | <50><br>( 0%)  | 0  | <50><br>( 0%)    | 1  | <50><br>( 2%)  |   |
| liver          | hepatocellular adenoma         |                                       | 0  | <50><br>( 0%)  | 2  | <50><br>( 4%)  | 1  | <50><br>( 2%)    | 0  | <50><br>( 0%)  |   |
|                | hepatocellular carcinoma       |                                       | 1  | ( 2%)          | 0  | ( 0%)          | 0  | ( 0%)            | 0  | ( 0%)          |   |
| pancreas       | islet cell adenoma             |                                       | 4  | <50><br>( 8%)  | 0  | <49><br>( 0%)  | 1  | <50><br>( 2%)    | 2  | <50><br>( 4%)  |   |
|                | islet cell adenocarcinoma      |                                       | 2  | ( 4%)          | 0  | ( 0%)          | 0  | ( 0%)            | 0  | ( 0%)          |   |
| {Urinary syste | em)                            |                                       |    |                |    |                |    |                  |    |                |   |
| kidney         | renal cell adenoma             |                                       | 0  | <50><br>( 0%)  | 0  | <50><br>( 0%)  | C  | <50><br>( 0%)    | 1  | <50><br>( 2%)  |   |
| urin bladd     | transitional cell papilloma    |                                       | 1  | <50><br>( 2%)  | 0  | <50><br>( 0%)  | C  | <50><br>( 0%)    | 1  | <50><br>( 2%)  |   |
|                | transitional cell carcinoma    |                                       | 0  | ( 0%)          | 0  | ( 0%)          | C  | ( 0%)            | 1  | ( 2%)          |   |
| {Endocrine sys | stem}                          |                                       |    |                |    |                |    |                  |    |                |   |
| pituitary      | adenoma                        |                                       | 11 | <50><br>( 22%) | 10 | <50><br>( 20%) | ę  | <50><br>( 18%)   | 11 | <50><br>( 22%) |   |
|                | adenocarcinoma                 |                                       | 0  | ( 0%)          | 1  | ( 2%)          | (  | ) ( 0%)          | 2  | ( 4%)          |   |
| thyroid        | C-cell adenoma                 |                                       | 14 | <50><br>(28%)  | 17 | <50><br>( 34%) | 15 | <50><br>5 ( 30%) | 14 | <50><br>( 28%) |   |

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

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

(HPT085)

| ANIMAL<br>REPORT TYPE | : 0342<br>: RAT F344/DuCrj<br>: A1<br>: MALE | $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | GE: 4           |                 |                 |                 |  |
|-----------------------|----------------------------------------------|--------------------------------------------------------|-----------------|-----------------|-----------------|-----------------|--|
| Organ                 | Findings                                     |                                                        |                 |                 |                 |                 |  |
| {Endocrine s          | system)                                      |                                                        |                 |                 |                 |                 |  |
| thyroid               | follicular adenoma                           |                                                        |                 |                 |                 |                 |  |
|                       | C-cell carcinoma                             |                                                        | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         | 1 ( 2%)         |  |
|                       | follicular adenocarcinoma                    |                                                        | 0 ( 0%)         | 1 ( 2%)         | 0 ( 0%)         | 4 ( 8%)         |  |
| adrenal               | pheochromocytoma                             |                                                        |                 |                 |                 |                 |  |
|                       | ganglioneuroma                               |                                                        | 0 ( 0%)         | 1 (2%)          | 0 ( 0%)         | 0 ( 0%)         |  |
|                       | pheochromocytoma:malignant                   |                                                        | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         | 1 ( 2%)         |  |
| {Reproductiv          | /e system)                                   |                                                        |                 |                 |                 |                 |  |
| testis                | interstitial cell tumor                      |                                                        |                 |                 |                 |                 |  |
|                       | rete testis adenoma                          |                                                        | 1 (2%)          | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         |  |
| mammary gl            | adenoma                                      |                                                        | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) |  |
|                       | fibroadenoma                                 |                                                        | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)         | 6 (12%)         |  |
| prep/cli gl           | adenoma                                      |                                                        | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |  |
|                       | adenocarcinoma                               |                                                        | 0 ( 0%)         | 1 ( 2%)         | 2 ( 4%)         | 0 ( 0%)         |  |

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

(HPT085)

BAIS3

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

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|                 |                         | Group Name                            |   | 0 ppm         | 3 ppm |               |    | 10 ppm        |    | 30 ppm        |
|-----------------|-------------------------|---------------------------------------|---|---------------|-------|---------------|----|---------------|----|---------------|
| )rgan           | Findings                | No. of animals on Study               |   | 50            |       | 50            |    | 50 50         |    | 50            |
| Vervous syst    | tem)                    |                                       |   |               |       |               |    |               |    |               |
| rain            |                         |                                       |   | <50>          |       | <50>          |    | <50>          |    | <50>          |
|                 | malignant reticulosis   |                                       |   | (2%)          | 0     | ( 0%)         | 0  | ( 0%)         | 0  | ( 0%)         |
|                 | glioma                  |                                       | 0 | ( 0%)         | 0     | ( 0%)         | 0  | ( 0%)         | 2  | ( 4%)         |
| Special sens    | se organs/appendage}    |                                       |   |               |       |               |    |               |    |               |
| ymbal <u>gl</u> |                         |                                       |   | <50>          |       | <50>          |    | <50>          |    | <50>          |
|                 | squamous cell papilloma |                                       | 0 | ( 0%)         | 0     | ( 0%)         | 0  | ( 0%)         | 1  | (2%)          |
|                 | carcinoma               |                                       | 0 | ( 0%)         | 1     | ( 2%)         | 1  | ( 2%)         | 1  | ( 2%)         |
| lusculoskele    | etal system}            |                                       |   |               |       |               |    |               |    |               |
| iscle           |                         | · · · · · · · · · · · · · · · · · · · |   | <50>          |       | <50>          |    | <50>          |    | <50>          |
|                 | sarcoma:NOS             |                                       | 0 | ( 0%)         | 0     | ( 0%)         | 1  | (2%)          | 0  | ( 0%)         |
| one             | chondroma               |                                       |   | <50>          |       | <50>          |    | <50>          |    | <50>          |
|                 |                         |                                       | 0 | ( 0%)         | 0     | ( 0%)         | 0  | ( 0%)         | 1  | (2%)          |
| ody cavitie     | 25)                     |                                       |   |               |       |               |    |               |    |               |
| eritoneum       | mesothelioma            |                                       |   | <50><br>( 4%) | 0     | <50>          | 10 | <50>          |    | <50>          |
| etroperit       |                         |                                       |   |               | 3     | ( 6%)         | 12 | (24%)         | 22 | ( 44%)        |
| rrober 1 f      | schwannoma:malignant    |                                       |   | <50><br>( 0%) | 0     | <50><br>( 0%) | 0  | <50><br>( 0%) | 1  | <50><br>( 2%) |
|                 | sarcoma:NOS             |                                       | 1 | (2%)          |       | ( 0%)         |    | ( 0%)         |    | ( 0%)         |

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

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

(HPT085)

BAIS3

APPENDIX L 2

## HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE

(2-YEAR STUDY)

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

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| REPORT TYPE :<br>SEX : | A1<br>FEMALE                   |                                       |                 |                 |                 | PAGE             |
|------------------------|--------------------------------|---------------------------------------|-----------------|-----------------|-----------------|------------------|
| Organ                  | Findings                       | Group Name<br>No. of animals on Study | 0 ppm<br>50     | 3 ppm<br>50     | 10 ppm<br>49    | 30 ppm<br>50     |
| {Integumentar;         | y system/appandage)            |                                       |                 |                 |                 |                  |
| skin/app               | squamous cell papilloma        |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <49><br>0 ( 0%) | <50><br>1 ( 2%)  |
|                        | keratoacanthoma                |                                       | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         | 1 ( 2%)          |
|                        | trichoepithelioma:malignant    |                                       | 1 (2%)          | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)          |
| subcutis               | fibroma                        |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <49><br>0 ( 0%) | <50><br>2 ( 4%)  |
|                        | schwannoma                     |                                       | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)          |
| {Respiratory           | system}                        |                                       |                 |                 |                 |                  |
| nasal cavit            | adenoma                        |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <49><br>4 ( 8%) | <50><br>8 ( 16%) |
|                        | squamous cell carcinoma        |                                       | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)         | 2 ( 4%)          |
|                        | adenocarcinoma                 |                                       | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)         | 2 ( 4%)          |
| lung                   | bronchiolar-alveolar adenoma   |                                       | <50><br>1 ( 2%) | <50><br>1 ( 2%) | <49><br>1 ( 2%) | <50><br>2 ( 4%)  |
|                        | bronchiolar-alveolar carcinoma |                                       | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         | 0 ( 0%)          |
| {Hematopoieti          | ic system)                     |                                       |                 |                 |                 |                  |
| lymph node             | malignant lymphoma             |                                       | <50><br>0 ( 0%) | <50><br>O ( 0%) | <49><br>1 ( 2%) | <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)

BAIS3

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

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| Organ         | Findings                       | Group Name<br>No. of animals on Study |   | 0 ppm<br>50   |   | 3 ppm<br>50   |   | 10 ppm<br>49  | 3 | 30 ppm<br>50  |
|---------------|--------------------------------|---------------------------------------|---|---------------|---|---------------|---|---------------|---|---------------|
| {Hematopoieti | c system)                      |                                       |   |               |   |               |   |               |   |               |
| spleen        | osteosarcoma                   |                                       |   | <50><br>( 0%) | 0 | <50><br>( 0%) | 1 | <49><br>( 2%) |   | <50><br>( 0%) |
|               | mononuclear cell leukemia      |                                       | 3 | ( 6%)         | 3 | ( 6%)         | 1 | ( 2%)         | 8 | ( 16%)        |
| {Digestive sy | stem)                          |                                       |   |               |   |               |   |               |   |               |
| cral cavity   | squamous cell papilloma        |                                       |   | <50><br>( 0%) | 0 | <50><br>( 0%) | 1 | <49><br>( 2%) | 0 | <50><br>( 0%) |
| tongue        | squamous cell papilloma        |                                       | 0 | <50><br>( 0%) | 1 | <50><br>( 2%) | 1 | <49><br>( 2%) | 1 | <50><br>( 2%) |
| stomach       | squamous cell papilloma        |                                       | 1 | <50><br>( 2%) | 0 | <50><br>( 0%) | 0 | <49><br>( 0%) | 2 | <50><br>( 4%) |
| small intes   | adenocarcinoma                 |                                       | 0 | <50><br>( 0%) | 0 | <50><br>( 0%) | 0 | <49><br>( 0%) | 1 | <50><br>( 2%) |
|               | malignant fibrous histiocytoma |                                       | 0 | ( 0%)         | 0 | ( 0%)         | 0 | ( 0%)         | 1 | ( 2%)         |
| pancreas      | islet cell adenoma             |                                       | 1 | <50><br>( 2%) | 1 | <50><br>( 2%) | 0 | <49><br>( 0%) | 0 | <50><br>( 0%) |
|               | acinar cell adenocarcinoma     |                                       | 1 | ( 2%)         | 0 | ( 0%)         | 0 |               | 1 | ( 2%)         |
| {Urinary syst | em)                            |                                       |   |               |   |               |   |               |   |               |
| kidney        | hemangiosarcoma                | ·                                     | 0 | <50><br>( 0%) | 1 | <50><br>( 2%) | 0 | <49><br>( 0%) | 0 | <50><br>( 0%) |
|               | nephroblastoma                 |                                       | 0 | ( 0%)         | 1 | ( 2%)         | 0 | ( 0%)         | 0 | ( 0%)         |

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

b (c) b : Number of animals with neoplasm c:b/a\*100 PAGE : 7

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

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| gan           | Findings                    | Group Name<br>No. of animals on Study |   | 0 ppm<br>50    |    | 3 ppm<br>50    |    | 10 ppm<br>49   |    | 30 ppm<br>50   |  |
|---------------|-----------------------------|---------------------------------------|---|----------------|----|----------------|----|----------------|----|----------------|--|
| lrinary syste | m)                          |                                       |   |                |    |                |    |                |    |                |  |
| in bladd      | transitional cell papilloma |                                       |   | <50><br>(2%)   | 1  | <50><br>( 2%)  | 0  | <49><br>( 0%)  | 0  | <50><br>( 0%)  |  |
| indocrine sys | tem)                        |                                       |   |                |    |                |    |                |    |                |  |
| tuitary       | adenoma                     | 1                                     |   | <50><br>( 26%) | 12 | <50><br>( 24%) | 15 | <49><br>( 31%) | 10 | <50><br>( 20%) |  |
|               | adenocarcinoma              |                                       | 2 | ( 4%)          | 4  | ( 8%)          | 1  | ( 2%)          | 1  | ( 2%)          |  |
| yroid         | C-cell adenoma              |                                       |   | <50><br>( 18%) | 5  | <50><br>( 10%) | 8  | <49><br>( 16%) | 7  | <50><br>( 14%) |  |
|               | follicular adenoma          |                                       | 0 | ( 0%)          | 1  | ( 2%)          | 0  | ( 0%)          | 0  | ( 0%)          |  |
|               | C-cell carcinoma            |                                       | 0 | ( 0%)          | 0  | ( 0%)          | 0  | ( 0%)          | 1  | ( 2%)          |  |
| renal         | pheochromocytoma            |                                       | 3 | <50><br>( 6%)  | 3  | <50><br>( 6%)  | 1  | <49><br>( 2%)  | 0  | <50><br>( 0%)  |  |
|               | cortical adenoma            |                                       | 0 | ( 0%)          | 0  | ( 0%)          | 2  | ( 4%)          | 0  | ( 0%)          |  |
|               | sarcoma:NOS                 |                                       | 0 | ( 0%)          | 0  | ( 0%)          | 1  | ( 2%)          | 0  | ( 0%)          |  |
|               | pheochromocytoma:malignant  |                                       | 0 | ( 0%)          | 2  | ( 4%)          | 0  | ( 0%)          | 0  | ( 0%)          |  |
| Reproductive  | system}                     |                                       |   |                |    |                |    |                |    |                |  |
| ary           | hemangioma                  |                                       | 0 | <50><br>( 0%)  | 0  | <50><br>( 0%)  | 0  | <49><br>( 0%)  | 1  | <50><br>( 2%)  |  |

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

(HPT085)

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

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| ;an          |                             | roup Name<br>o. of animals on Study |   | 0 ppm<br>50    |     | 3 ppm<br>50    |    |            | ) ppm<br>49    |    | 30 ppm<br>50  |
|--------------|-----------------------------|-------------------------------------|---|----------------|-----|----------------|----|------------|----------------|----|---------------|
| eproductive  | system)                     |                                     |   |                |     |                |    |            |                |    |               |
| ary          | sertoli cell tumor          | 1                                   |   | <50><br>( 2%)  | 0   | <50><br>(0%)   | 0  |            | <49><br>( 0%)  | 0  | <50><br>( 0%) |
|              | granulosa-theca cell tumor  | 0                                   | ) | ( 0%)          | 1   | ( 2%)          | 0  | ) (        | ( 0%)          | 0  | ( 0%)         |
| erus         | endometrial stromal polyp   | 6                                   |   | <50><br>( 12%) | 11  | <50><br>( 22%) | 11 |            | <49><br>( 22%) | 13 | <50><br>(26%) |
|              | adenocarcinoma              | 0                                   | ) | ( 0%)          | 0   | ( 0%)          | 3  | <b>;</b> - | ( 6%)          | 0  | ( 0%)         |
|              | hemangiosarcoma             | 0                                   | ) | ( 0%)          | 0   | ( 0%)          | 0  | )          | ( 0%)          | 1  | (2%)          |
|              | endometrial stromal sarcoma | 1                                   | 1 | (2%)           | 4   | ( 8%)          | 4  | 1          | ( 8%)          | 7  | ( 14%)        |
| gina         | hemangioma                  | 0                                   |   | <50><br>( 0%)  | 0   | <50><br>( 0%)  | 0  |            | <49><br>( 0%)  | 1  | <50><br>( 2%) |
|              | hemangiosarcoma             | 0                                   | 0 | ( 0%)          | 0   | ( 0%)          | 1  | L          | ( 2%)          | 0  | ( 0%)         |
| nmary gl     | adenoma                     | . 2                                 |   | <50><br>( 4%)  | 1   | <50><br>( 2%)  | 3  |            | <49><br>( 6%)  | 2  | <50><br>( 4%) |
|              | fibroadenoma                | 8                                   | 8 | (16%)          | 6   | ( 12%)         | 18 | 3          | ( 37%)         | 17 | ( 34%)        |
|              | adenocarcinoma              | 2                                   | 2 | ( 4%)          | 1   | ( 2%)          | 1  | L          | ( 2%)          | 2  | ( 4%)         |
| ep/cli gl    | adenoma                     | · C                                 |   | <50><br>( 0%)  | 0   | <50><br>( 0%)  | с  |            | <49><br>( 0%)  | 2  | <50><br>( 4%) |
| ervous syste | em)                         |                                     |   |                |     |                |    |            |                |    |               |
| ain          | glioma                      |                                     |   | <50><br>( 0%)  | . 0 | <50><br>( 0%)  | (  |            | <49><br>( 0%)  | 1  | <50><br>( 2%) |

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

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

(HPT085)

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

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| Organ           | Findings             | Group Name<br>No. of animals on Study | 0 ppm<br>50     | 3 ppm<br>50     | 10 ppm<br>49    | 30 ppm<br>50    |
|-----------------|----------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
|                 |                      |                                       |                 | <u> </u>        |                 |                 |
| {Nervous system | a}                   |                                       |                 |                 |                 |                 |
| orain           | meningiome:malignant |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <49><br>1 ( 2%) | <50><br>0 ( 0%) |
| {Special sense  | organs/appendage)    |                                       |                 |                 |                 |                 |
| Zymbal gl       | carcinoma            |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <49><br>1 ( 2%) | <50><br>0 ( 0%) |
| {Musculoskelet  | al system)           |                                       |                 |                 |                 |                 |
| bone            | osteoma              |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <49><br>0 ( 0%) | <50><br>1 ( 2%) |
| (Body cavities) | )                    |                                       |                 |                 |                 |                 |
| peritoneum      | fibroma              |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <49><br>1 ( 2%) | <50><br>0 ( 0%) |
|                 | mesothelioma         |                                       | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         | 0 ( 0%)         |

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

(HPT085)

APPENDIX M 1

# NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL

ANALYSIS, RAT : MALE

(2-YEAR STUDY)

| Group Name                                       | 0 ppm  | 3 ppm              | 10 ppm              | 30 ppm              |  |
|--|--|--------------------|---------------------|---------------------|--|
|  | SITE : skin/appendage                            |                    |                     |                     |  |
| mor rate   | TUMOR : squamous cell papilloma                  |                    |                     |                     |  |
| Overall rates(a)                                 | 0/50( 0.0)                                       | 0/50( 0.0)         | 1/50(2,0)           | 3/50( 6.0)          |  |
| Adjusted rates(b)                                | 0,0  | 0,0                | 2.63                | 8.70                |  |
| ferminal rates(c)<br>tatistical analysis         | 0/40( 0.0)                                       | 0/42( 0.0)         | 1/38( 2,6)          | 2/23( 8.7)          |  |
| Peto test<br>Standard method(d)                  | P =  |                    |                     |                     |  |
| Prevalence method(d)                             | P = 0.0069 * *                                   |                    |                     |                     |  |
| Combined analysis(d)                             | P =  |                    |                     |                     |  |
| Cochran-Armitage test(e)                         | P = 0.0138*                                      |                    |                     |                     |  |
| Fisher Exact test(e)                             |  | P = N. C.          | P = 0.5000          | P = 0.1212          |  |
|  |  |                    |                     |                     |  |
|  | SITE : skin/appendage<br>TUMOR : keratoacanthoma |                    |                     |                     |  |
| umor rate  | TOMOR · Relatoacanthona                          |                    |                     |                     |  |
| Overall rates(a)                                 | 3/50( 6.0)                                       | 3/50( 6.0)         | 0/50(0.0)           | 2/50( 4.0)          |  |
| Adjusted rates(b)                                | 7.50   | 4. 76              | 0, 0                | 8.70                |  |
| Terminal rates(c)                                | 3/40(7.5)  | 2/42( 4.8)         | 0/38( 0.0)          | 2/23( 8.7)          |  |
| tatistical analysis                              |  |                    |                     |                     |  |
| Peto test  |  |                    |                     |                     |  |
| Standard method(d)                               | P = 0.5196                                       |                    |                     |                     |  |
| Prevalence method(d)                             | P = 0.3621                                       |                    |                     |                     |  |
| Combined analysis(d)<br>Cochran-Armitage test(e) | P = 0.4613<br>P = 0.5998                         |                    |                     |                     |  |
| Fisher Exact test(e)                             | r – 0. 5556                                      | P = 0.6611         | P = 0.1212          | P = 0.5000          |  |
|  |  |                    |                     |                     |  |
|  | SITE : subcutis                                  |                    |                     |                     |  |
|  | TUMOR : fibroma                                  |                    |                     |                     |  |
| umor rate  |  |                    |                     |                     |  |
| Overall rates(a)                                 | 10/50(20.0)                                      | 2/50( 4.0)         | 10/50(20.0)         | 9/50(18.0)<br>21.74 |  |
| Adjusted rates(b)<br>Terminal rates(c)           | 20.00<br>8/40(20.0)                              | 4.76<br>2/42( 4.8) | 19.15<br>7/38(18.4) | 5/23(21.7)          |  |
| statistical analysis                             | 8/40(20.0)                                       | 2/42( 4.8)         | 1/36(18.4)          | 5/25(21.7)          |  |
| Peto test  |  |                    |                     |                     |  |
| Standard method(d)                               | P = 0.8433                                       |                    |                     |                     |  |
| Prevalence method(d)                             | P = 0.1043                                       |                    |                     |                     |  |
| Combined analysis(d)                             | P = 0.1927                                       |                    |                     |                     |  |
|  |  |                    |                     |                     |  |
| Cochran-Armitage test(e)<br>Fisher Exact test(e) | P = 0.4750                                       | P = 0,0139*        | P = 0.5984          | P = 0.5000          |  |

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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PAGE : 1

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Group Name

0 ppm

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

3 ppm

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10 ppm

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| $\begin{array}{c} \text{SITE : subcutis} \\ \text{TUMOR : fibroms, fibrosercoms} \end{array} \\ \hline \text{Tumor rate} \\ \hline \text{Overall rates(a)} & 10/50(20.0) & 2/50(4.0) & 10/50(20.0) & 10/50(20.0) \\ \text{Adjusted rates(b)} & 20.00 & 4.76 & 19.15 & 23.08 \\ \hline \text{Terminal rates(c)} & 8/40(20.0) & 2/42(4.8) & 7/38(18.4) & 5/23(21.7) \\ \hline \text{Statistical analysis} \\ \text{Peto test} \\ \hline \text{Standard method(d)} & P = 0.8433 \\ \text{Prevalence method(d)} & P = 0.3064 \\ \hline \text{Fisher Exact test(e)} & P = 0.3064 \\ \hline \text{Fisher Exact test(e)} & P = 0.3064 \\ \hline \text{Fisher Exact test(e)} & P = 0.0139 \star & P = 0.5984 \\ \hline \text{SITE : nasal cavity} \\ \hline \text{TUMOR : adenoms} \\ \hline \text{Tumor rate} \\ \hline \text{Overall rates(b)} & 0/50(0.0) & 0/50(0.0) & 3/50(6.0) & 5/50(10.0) \\ \hline \text{Adjusted rates(b)} & 0.0 & 0 & 0.0 \\ \hline \text{Terminal rates(c)} & 0/40(0.0) & 0/42(0.0) & 3/38(7.9) & 4/23(17.4) \\ \hline \end{array}$ |          |
|---|----------|
| Tumor rate $2/50(4.0)$ $10/50(20.0)$ $10/50(20.0)$ Adjusted rates(b) $20.00$ $4.76$ $19.15$ $23.08$ Terminal rates(c) $8/40(20.0)$ $2/42(4.8)$ $7/38(18.4)$ $5/23(21.7)$ Statistical analysis       Peto test $5/23(21.7)$ $5/23(21.7)$ Standard method(d)       P = 0.8433       Prevalence method(d)       P = 0.8433         Prevalence method(d)       P = 0.1201 $Cochran-Armitage test(e)$ P = 0.139*       P = 0.5984         Fisher Exact test(e)       P = 0.0139*       P = 0.5984       P = 0.5984       P = 0.5984         Tumor rate         Overall rates(s) $0/50(0.0)$ $0/50(0.0)$ $3/50(6.0)$ $5/50(10.0)$ Advance         Tumor rate         Coreral rates(s) $0/50(0.0)$ $0/50(0.0)$ $3/50(6.0)$ $5/50(10.0)$ Advance         SITE : nasal cavity         Tumor rate $0.00$ $0.00$ $3/50(6.0)$ $5/50(10.0)$ Advance         Tumor rate         Tumor rate       Overall rates(s)       <   |          |
| Overall rates(a) $10/50(20.0)$ $2/50(4.0)$ $10/50(20.0)$ $10/50(20.0)$ Adjusted rates(b) $20.00$ $4.76$ $19.15$ $23.08$ Terminal rates(c) $8/40(20.0)$ $2/42(4.8)$ $7/38(18.4)$ $5/23(21.7)$ Statistical analysis $7/38(18.4)$ $5/23(21.7)$ $5/23(21.7)$ Peto test $5/20(20.0)$ $2/42(4.8)$ $7/38(18.4)$ $5/23(21.7)$ Statistical analysis $P = 0.8433$ $P = 0.0578$ $P = 0.0578$ Combined analysis(d) $P = 0.1201$ $P = 0.0139*$ $P = 0.5984$ $P = 0.5984$ Fisher Exact test(e) $P = 0.0139*$ $P = 0.5984$ $P = 0.5984$ Tumor rate         Overall rates(b) $0/50(0.0)$ $0/50(0.0)$ $3/50(6.0)$ $5/50(10.0)$ Adjusted rates(b) $0.0$ $0.0$ $7.89$ $17.39$ Terminal rates(c) $0/40(0.0)$ $0/42(0.0)$ $3/38(7.9)$ $4/23(17.4)$   |          |
| Adjusted rates (b)       20.00       4.76       19.15       23.08         Terminal rates(c) $8/40(20.0)$ $2/42(4.8)$ $7/38(18.4)$ $5/23(21.7)$ Statistical analysis       Peto test $5$ $5/23(21.7)$ Standard method(d)       P = 0.8433       Prevalence method(d)       P = 0.0578         Combined analysis(d)       P = 0.1201       Cochran-Amitage test(e)       P = 0.0139*         Fisher Exact test(e)       P = 0.0139*       P = 0.5984       P = 0.5984         SITE : nasal cavity         TUMOR : adenoma $0/50(0.0)$ $0/50(0.0)$ $3/50(6.0)$ $5/50(10.0)$ Adjusted rates(b)       0.0       0.0       7.89       17.39         Terminal rates(c) $0/40(0.0)$ $0/42(0.0)$ $3/38(7.9)$ $4/23(17.4)$  |          |
| Terminal rates(c) $8/40(20.0)$ $2/42(4.8)$ $7/38(18.4)$ $5/23(21.7)$ Statistical analysis       Peto test       Standard method(d) $P = 0.8433$ Prevelence method(d) $P = 0.0578$ Combined analysis(d) $P = 0.1201$ Cochran-Armitage test(e) $P = 0.3064$ $P = 0.0139*$ $P = 0.5984$ $P = 0.5984$ Fisher Exact test(e) $P = 0.0139*$ $P = 0.5984$ $P = 0.5984$ Tumor rate         Overall rates(a) $0/50(0.0)$ $0/50(0.0)$ $3/50(6.0)$ $5/50(10.0)$ Adjusted rates(b) $0.0$ $0.0$ $7.89$ $17.39$ Terminal rates(c) $0/40(0.0)$ $0/42(0.0)$ $3/38(7.9)$ $4/23(17.4)$   |          |
| Statistical analysis         Peto test         Standard method(d) $P = 0.8433$ Prevalence method(d) $P = 0.0578$ Combined analysis(d) $P = 0.1201$ Cochran-Armitage test(e) $P = 0.3064$ Fisher Exact test(e) $P = 0.0139*$ $P = 0.5984$ SITE : nasal cavity         TUMOR : adenoma         Tumor rate         Overall rates(a) $0/50(0.0)$ $0/50(0.0)$ $3/50(6.0)$ $5/50(10.0)$ Adjusted rates(b) $0.0$ $0.0$ $7.89$ $17.39$ Terminal rates(c) $0/40(0.0)$ $0/42(0.0)$ $3/38(7.9)$ $4/23(17.4)$   |          |
| Peto       test         Standard method(d) $P = 0.8433$ Prevalence method(d) $P = 0.0578$ Combined analysis(d) $P = 0.1201$ Cochran-Armitage test(e) $P = 0.3064$ Fisher Exact test(e) $P = 0.0139*$ P = 0.5984 $P = 0.5984$ SITE : nasal cavity<br>TUMOR : adenoma         Tumor rate         Overall rates(a) $0/50(0.0)$ $0/50(0.0)$ $3/50(6.0)$ $5/50(10.0)$ Adjusted rates(b) $0.0$ $0.0$ $7.89$ $17.39$ Terminal rates(c) $0/40(0.0)$ $0/42(0.0)$ $3/38(7.9)$ $4/23(17.4)$  |          |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$  |          |
| Prevalence method(d) $P = 0.0578$ Combined analysis(d) $P = 0.1201$ Cochran-Armitage test(e) $P = 0.3064$ Fisher Exact test(e) $P = 0.0139*$ $P = 0.5984$ SITE       : nasal cavity<br>TUMOR       : adenoma         Tumor rate $0/50(0.0)$ $0/50(0.0)$ $3/50(6.0)$ $5/50(10.0)$ Overall rates(a) $0/50(0.0)$ $0/0$ $7.89$ $17.39$ Terminal rates(c) $0/40(0.0)$ $0/42(0.0)$ $3/38(7.9)$ $4/23(17.4)$   |          |
| Combined analysis(d) $P = 0.1201$ Cochran-Armitage test(e) $P = 0.3064$ Fisher Exact test(e) $P = 0.0139*$ $P = 0.5984$ SITE       : nasal cavity         TUMOR       : adenoma         Tumor rate $0/50(0.0)$ $0/50(0.0)$ $3/50(6.0)$ $5/50(10.0)$ Overall rates(a) $0/50(0.0)$ $0/0$ $7.89$ $17.39$ Terminal rates(c) $0/40(0.0)$ $0/42(0.0)$ $3/38(7.9)$ $4/23(17.4)$  |          |
| Cochran-Armitage test(e)       P = 0.3064       P = 0.0139*       P = 0.5984       P = 0.5984         SITE : nasal cavity         TUMOR : adenoma         Tumor rate         Overall rates(a)       0/50(0.0)       0/50(0.0)       3/50(6.0)       5/50(10.0)         Adjusted rates(b)       0.0       7.89       17.39         Terminal rates(c)       0/40(0.0)       0/42(0.0)       3/38(7.9)       4/23(17.4)  |          |
| Fisher Exact test(e)       P = 0.0139*       P = 0.5984       P = 0.5984         SITE : nasal cavity<br>TUMOR : adenoma         Tumor rate       0/50(0.0)       0/50(0.0)       3/50(6.0)       5/50(10.0)         Adjusted rates(b)       0.0       0.0       7.89       17.39         Terminal rates(c)       0/40(0.0)       0/42(0.0)       3/38(7.9)       4/23(17.4)   |          |
| SITE : nasal cavity<br>TUMOR : adenoma         Tumor rate         Overall rates(a)       0/50(0.0)       0/50(0.0)       3/50(6.0)       5/50(10.0)         Adjusted rates(b)       0.0       7.89       17.39         Terminal rates(c)       0/40(0.0)       0/42(0.0)       3/38(7.9)       4/23(17.4)   |          |
| TUMOR : adenoma         Tumor rate         Overall rates(a)       0/50(0.0)       0/50(0.0)       3/50(6.0)       5/50(10.0)         Adjusted rates(b)       0.0       0.0       7.89       17.39         Terminal rates(c)       0/40(0.0)       0/42(0.0)       3/38(7.9)       4/23(17.4)  | <u> </u> |
| Tumor rate         Overall rates (a)         0/50(0.0)         0/50(0.0)         3/50(6.0)         5/50(10.0)           Adjusted rates (b)         0.0         0.0         7.89         17.39           Terminal rates (c)         0/40(0.0)         0/42(0.0)         3/38(7.9)         4/23(17.4)   |          |
| Overall rates(a)         0/50(0.0)         0/50(0.0)         3/50(6.0)         5/50(10.0)           Adjusted rates(b)         0.0         0.0         7.89         17.39           Terminal rates(c)         0/40(0.0)         0/42(0.0)         3/38(7.9)         4/23(17.4)   |          |
| Adjusted         rates(b)         0.0         7.89         17.39           Terminal         rates(c)         0/40(0.0)         0/42(0.0)         3/38(7.9)         4/23(17.4)   |          |
| Terminal rates(c) 0/40(0.0) 0/42(0.0) 3/38(7.9) 4/23(17.4)  |          |
|   |          |
| Statical applycic   |          |
| oranorian anaroto   |          |
| Peto test   |          |
| Standard method (d) $P =$   |          |
| Prevalence method(d) P = 0.0006**   |          |
| Combined analysis(d) P =  |          |
| Cochran-Armitage test(e) P = 0.0037**   |          |
| Fisher Exact test(e) $P = N. C.$ $P = 0.1212$ $P = 0.0281*$   |          |
|   |          |
| SITE : nasal cavity   |          |
| TUMOR : squamous cell carcinoma   |          |
| Tumor rate  |          |
| Overall rates (a)         0/50(0.0)         0/50(0.0)         0/50(0.0)         14/50(28.0)   |          |
| Adjusted rates(b) 0.0 0.0 0.0 34.78   |          |
| Terminal rates(c)         0/40(0.0)         0/42(0.0)         0/38(0.0)         8/23(34.8)  |          |
| Statistical analysis  |          |
| Peto test   |          |
| Standard method (d) P < 0.0001**?   |          |
| Prevalence method(d) P < 0.0001**?<br>Combined analysis(d) P < 0.0001**?  |          |
| Combined analysis(d) P < 0.0001**?<br>Cochran-Armitage test(e) P < 0.0001**   |          |
| Fisher Exact test(e) P < 0.0001** P = N.C. P = N.C. P < 0.0001**  |          |
|   |          |

PAGE: 2

30 ppm

| TUDY No. : 0342<br>NIMAL : RAT F344/DuCrj   |   | NEOPLASTIC LESIONS-INCIDENCE AND STAT                     | TISTICAL ANALYSIS                                       |   |        |
|---|---|---|---|---|--------|
| EX : MALE   |   |   |   |   | PAGE : |
| Group Name  | 0 ppm   | 3 ppm   | 10 ppm  | 30 ppm  |        |
|   | SITE : nasal cavity<br>TUMOR : adenoma,adenocarcinom  | a   |   |   |        |
| Tumor rate  |   |   |   |   |        |
| Overall rates(a)  | 0/50( 0.0)  | 0/50( 0.0)  | 3/50( 6.0)  | 6/50(12.0)                                      |        |
| Adjusted rates(b)   | 0.0   | 0.0   | 7.89  | 21.74   |        |
| Terminal rates(c)<br>Statistical analysis<br>Peto test  | 0/40( 0.0)  | 0/42( 0.0)  | 3/38(7.9)   | 5/23(21.7)                                      |        |
| Standard method(d)  | P =   |   |   |   |        |
| Prevalence method(d)  | P = 0.0001**  |   |   |   |        |
| Combined analysis(d)  | P =   |   |   |   |        |
| Cochran-Armitage test(e)<br>Fisher Exact test(e)  | P = 0.0010**  | P = N. C.   | P = 0.1212  | P = 0.0133*                                     |        |
| Tumor rate<br>Overall rates(a)<br>Adjusted rates(b)<br>Terminal rates(c)<br>Statistical analysis<br>Peto test<br>Standard method(d)<br>Prevalence method(d)<br>Combined analysis(d)<br>Cochran-Armitage test(e)<br>Fisher Exact test(e) | SITE : lung<br>TUMOR : bronchiolar-alveolar<br>2/50( 4.0)<br>4.76<br>1/40( 2.5)<br>P =<br>P = 0.3220<br>P =<br>P = 0.9716 | adenoma<br>4/50( 8.0)<br>8.33<br>3/42( 7.1)<br>P = 0.3389 | 5/50 ( 10. 0)<br>13. 16<br>5/38 ( 13. 2)<br>P = 0. 2180 | 3/50( 6.0)<br>10.34<br>2/23( 8.7)<br>P = 0.5000 |        |
| Tumor voto  | SITE : lung<br>TUMOR : bronchiolar-alveolar   | carcinoma   |   |   |        |
| Tumor rate<br>Overall rates(a)  | 4/50 ( 8.0)   | 3/50( 6.0)  | 2/50( 4.0)  | 0/50( 0.0)                                      |        |
| Adjusted rates(b)   | 10.00   | 4.76  | 2,000 1.07  | 0.0   |        |
| Terminal rates(c)<br>Statistical analysis<br>Peto test  | 4/40( 10.0)   | 2/42( 4.8)  | 1/38( 2.6)  | 0/23( 0.0)                                      |        |
| Standard method(d)<br>Prevalence method(d)<br>Combined analysis(d)<br>Cochran-Armitage test(e)  | P = 0.5903<br>P = 0.9683<br>P = 0.9624<br>P = 0.0481*   |   |   |   |        |
| Fisher Exact test(e)  |   | P = 0.5000  | P = 0.3389  | P = 0.0587                                      |        |

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| STUDY No. : 0342<br>ANIMAL : RAT F344/DuCrj<br>SEX : MALE   |  | NEOPLASTIC LESIONS-INCIDENCE AND STA     | TISTICAL ANALYSIS                |                                     | PAGE : 4 |
|---|--|--|----------------------------------|-------------------------------------|----------|
| Group Name  | 0 ppm  | 3 ppm                                    | 10 ppm                           | 30 ppm                              |          |
|   | SITE : lung  |  |                                  | ·····                               |          |
| Tumor rate  | IUMOK : bronchiolar-alveolar   | adenoma, bronchiolar-alveolar carcinom   | a                                |                                     |          |
| Overall rates(a)  | 6/50(12.0)   | 7/50(14.0)                               | 7/50(14.0)                       | 3/50(6.0)                           |          |
| Adjusted rates(b)   | 14. 29   | 12. 77                                   | 15.79                            | 10.34                               |          |
| Terminal rates(c)   | 5/40(12.5)   | 5/42(11.9)                               | 6/38(15.8)                       | 2/23(8.7)                           |          |
| Statistical analysis  |  |  |                                  |                                     |          |
| Peto test   |  |  |                                  |                                     |          |
| Standard method(d)  | P = 0.5903   |  |                                  |                                     |          |
| Prevalence method(d)  | P = 0.7406   |  |                                  |                                     |          |
| Combined analysis(d)  | P = 0.7756   |  |                                  |                                     |          |
| Cochran-Armitage test(e)<br>Fisher Exact test(e)  | P = 0.2091   |  | D 0 5000                         | D 0.0405                            |          |
| Fisher Exact test(0)  |  | P = 0.5000                               | P = 0.5000                       | P = 0.2435                          |          |
| Tumor rate<br>Overall rates(a)<br>Adjusted rates(b)<br>Terminal rates(c)<br>Statistical analysis<br>Peto test<br>Standard method(d)<br>Prevalence method(d)<br>Combined analysis(d)<br>Cochran-Armitage test(e) | SITE : spleen<br>TUMOR : mononuclear cell leu<br>8/50(16.0)<br>7.50<br>3/40(7.5)<br>P = 0.6506<br>P = 0.0828<br>P = 0.2751<br>P = 0.9916 | kemia<br>1/50( 2.0)<br>0.0<br>0/42( 0.0) | 4/50( 8.0)<br>5.13<br>1/38( 2.6) | 5/50( 10.0)<br>13.04<br>3/23( 13.0) |          |
| Fisher Exact test(e)  |  | P = 0.0154*                              | P = 0.1783                       | P = 0.2768                          |          |
| Tumor rate<br>Overall rates(a)<br>Adjusted rates(b)<br>Terminal rates(c)<br>Statistical analysis<br>Peto test<br>Standard method(d)<br>Prevalence method(d)<br>Combined analysis(d)                             | SITE : pancreas<br>TUMOR : islet cell adenoma<br>4/50( 8.0)<br>10.00<br>4/40( 10.0)<br>P =<br>P = 0.3158<br>P =                          | 0/49( 0.0)<br>0.0<br>0/41( 0.0)          | 1/50( 2.0)<br>2.63<br>1/38( 2.6) | 2/50( 4.0)<br>8.70<br>2/23( 8.7)    |          |
| Cochran-Armitage test(e)  | P = 0.8560   |  |                                  |                                     |          |
| Fisher Exact test(e)  |  | P = 0.0612                               | P = 0.1811                       | P = 0.3389                          |          |

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| $\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$  | 8.70            |
|---|-----------------|
| $\begin{tabular}{l lllllllllllllllllllllllllllllllllll$   | 8.70            |
| Tumor rate $0/49(0,0)$ $1/50(2,0)$ $2/50(0,0)$ Adjusted rates(a) $6/50(12,0)$ $0/49(0,0)$ $1/50(2,0)$ $2/50(0,0)$ Adjusted rates(b) $15,00$ $0,0$ $2.63$ $2/23(0,0)$ Terminal rates(c) $6/40(15,0)$ $0/41(0,0)$ $1/38(2,6)$ $2/23(0,0)$ Statistical analysis       P =       Prevalence method(d)       P =         Combined analysis(d)       P =       Cohran-Armitage test(e)       P = $0.559$ P = $0.142*$ Cochran-Armitage test(e)       P = $0.4297$ P = $0.0142*$ P = $0.0559$ P = $0.1$ Value on the fourth of the fo  | 8.70            |
| Overall rates(a) $6/50(12.0)$ $0/49(0.0)$ $1/50(2.0)$ $2/50(2.0)$ Adjusted rates(b)       15.00 $0.0$ $2.63$ Terminal rates(c) $6/40(15.0)$ $0/41(0.0)$ $1/38(2.6)$ $2/23(2.6)$ Statistical analysis       Perovalence method(d) $P =$ Provalence method(d) $P =$ Provalence method(d) $P =$ Cochran-Armitage test(e) $P = 0.5440$ $P = 0.0142*$ $P = 0.0559$ $P = 0.1$ SITE       : pituitary gland       TUMOR       : adenome $P = 0.0142*$ $P = 0.0559$ $P = 0.1$ More rate       0verall rates(c)       9/50(18.0)       11/50(22.0)       10/50(20.0)       9/50(18.0)       11/50(21.0)         Adjusted rates(b)       22.50       23.81       21.95       11/50(22.5)       10/42(23.8)       7/38(18.4) $6/23(2.5)$ Statistical analysis       Peto test       Standard method(d) $P = 1.0000$ ?       Provalence method(d) $P = 0.2562$ Cochran-Armitage test(e) $P = 0.8898$  | 8.70            |
| Adjusted rates (b)       15.00       0.0       2.63         Terminal rates (c) $6/40(15.0)$ $0/41(0.0)$ $1/38(2.6)$ $2/23(5)$ Statistical analysis       Peto test       Standard method(d) $P =$ Prevalence method(d) $P =$ Combined analysis(d) $P =$ Cochran-Armitage test(e) $P = 0.5440$ Cochran-Armitage test(e) $P = 0.4297$ Fisher Exact test(e) $P = 0.4297$ $P = 0.0142*$ $P = 0.0559$ $P = 0.1$ SITE : pituitary gland         Tumor rate $VTMOR$ : adenoma $P = 0.0142*$ $P = 0.0559$ $P = 0.1$ Adjusted rates(a) $11/50(22.0)$ $10/50(20.0)$ $9/50(18.0)$ $11/50(20.0)$ Adjusted rates(b) $22.50$ $23.81$ $21.95$ $21.95$ Terminal rates(c) $9/40(22.5)$ $10/42(23.8)$ $7/38(18.4)$ $6/23(20.6)$ Statistical analysis $P = 1.0000$ ? $P = 0.2562$ $Cochran-Armitage test(e)$ $P = 0.2562$ Cochran-Armitage test(e) $P = 0.2562$ $Cochran-Armitage test(e)$ $P = 0.8888$  | 8.70            |
| Terminal rates(c) $6/40(15.0)$ $0/41(0.0)$ $1/38(2.6)$ $2/23(5)$ Statistical analysis       Peto test       Statistical analysis $2/23(5)$ Peto test       Statiatd method(d) $P =$ $2/23(5)$ Statiatd method(d) $P =$ $Peto test$ $2/23(5)$ Combined analysis(d) $P =$ $Peto test$ $P =$ Cochran-Armitage test(e) $P = 0.4297$ $P = 0.0142*$ $P = 0.0559$ $P = 0.12*$ SITE : pituitary gland       TUMOR : adenoma $TUMOR : adenoma$ $TUMOR : adenoma$ $11/50(22.0)$ $10/50(20.0)$ $9/50(18.0)$ $11/50(20.0)$ Overall rates(a) $11/50(22.0)$ $10/50(20.0)$ $9/50(18.0)$ $11/50(20.0)$ $11/50(2$  |                 |
| Statistical analysis<br>Peto test<br>Standard method(d) $P =$<br>Prevalence method(d) $P = 0.5440$<br>Combined analysis(d) $P =$<br>Cochran-Armitage test(e) $P = 0.4297$<br>Fisher Exact test(e) $P = 0.4297$<br>SITE : pituitary gland<br>TUMOR : adenome<br>Tumor rate<br>Overall rates(a) 11/50(22.0) 10/50(20.0) 9/50(18.0) 11/50(<br>Adjusted rates(b) 22.50 23.81 21.95<br>Terminal rates(c) 9/40(22.5) 10/42(23.8) 7/38(18.4) 6/23(<br>Statistical analysis<br>Peto test<br>Statistical analysis<br>Peto test<br>Standard method(d) $P = 1.0000$ ?<br>Prevalence method(d) $P = 0.2562$<br>Cochran-Armitage test(e) $P = 0.8898$  | 6.17            |
| $\begin{array}{cccc} Prevalence method(d) & P = 0.5440 \\ Combined analysis(d) & P = \\ Cochran-Armitage test(e) & P = 0.4297 \\ \hline Fisher Exact test(e) & P = 0.4297 \\ \hline Fisher Exact test(e) & P = 0.012* & P = 0.0559 & P = 0.1 \\ \hline & & & \\ & & & \\ \hline & & & \\ & & & \\ \hline & & & \\ \hline$ |                 |
| Combined analysis(d) $P =$ Cochran-Armitage test(e) $P = 0.4297$ Fisher Exact test(e) $P = 0.0142*$ $P = 0.0559$ $P = 0.1$ SITE : pituitary gland         TUMOR : adenoma         Tumor rate         Overall rates(a) $11/50(22.0)$ $10/50(20.0)$ $9/50(18.0)$ $11/50(21.0)$ Adjusted rates(b) $22.50$ $23.81$ $21.95$ $6/23(21.95)$ Terminal rates(c) $9/40(22.5)$ $10/42(23.8)$ $7/38(18.4)$ $6/23(23.6)$ Statistical analysis         Peto test       Standard method(d) $P = 0.2050$ $Combined analysis(d)$ $P = 0.2562$ Cochran-Armitage test(e) $P = 0.8398$  |                 |
| Cochran-Armitage test(e) $P = 0.4297$ Fisher Exact test(e) $P = 0.012*$ $P = 0.0559$ $P = 0.1$ SITE : pituitary gland<br>TUMOR : adenoma         Tumor rate         Overall rates(a)       11/50(22.0)       10/50(20.0)       9/50(18.0)       11/50(<br>Adjusted rates(b)         Z2.50       23.81       21.95         Terminal rates(c)       9/40(22.5)       10/42(23.8)       7/38(18.4)       6/23(<br>6/23(<br>5/23(5))         Statistical analysis<br>Peto test       Standard method(d) $P = 1.0000$ ?       Prevalence method(d) $P = 0.2562$ Conbined analysis(d) $P = 0.2562$ Cochran-Armitage test(e) $P = 0.8898$  |                 |
| Fisher Exact test(e) $P = 0.0142*$ $P = 0.0559$ $P = 0.1$ SITE : pituitary gland<br>TUMOR : adenoma         Tumor rate       0verall rates(a)       11/50(22.0)       10/50(20.0)       9/50(18.0)       11/50(<br>Adjusted rates(b)       22.50       23.81       21.95         Terminal rates(c)       9/40(22.5)       10/42(23.8)       7/38(18.4)       6/23(<br>Statistical analysis         Peto test       Standard method(d)       P = 1.0000 ?       Prevalence method(d)       P = 0.2050         Combined analysis(d)       P = 0.2562       Cochran-Armitage test(e)       P = 0.8898  |                 |
| $\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$  |                 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | 43              |
| Tumor rate       0verall rates (a) $11/50$ (22.0) $10/50$ (20.0) $9/50$ (18.0) $11/50$ (20.0)         Adjusted rates (b)       22.50       23.81       21.95         Terminal rates (c) $9/40$ (22.5) $10/42$ (23.8) $7/38$ (18.4) $6/23$ (20.0)         Statistical analysis       Peto test $7/38$ (18.4) $6/23$ (20.0)         Standard method(d)       P = 1.0000 ?       Prevalence method(d)       P = 0.2050         Combined analysis(d)       P = 0.2562       Cochran-Armitage test(e)       P = 0.8898   |                 |
| Adjusted rates (b)       22.50       23.81       21.95         Terminal rates (c) $9/40$ (22.5) $10/42$ (23.8) $7/38$ (18.4) $6/23$ (18.4)         Statistical analysis       Peto test $7/38$ (18.4) $6/23$ (18.4) $6/23$ (18.4)         Standard method (d)       P = 1.0000 ?       Prevalence method (d)       P = 0.2050 $6/23$ (18.4) $6/23$ (18.4)         Combined analysis (d)       P = 0.2050 $6/23$ (18.4) $6/23$ (18.4) $6/23$ (18.4)         Cochran-Armitage test (e)       P = 0.2562 $6/23$ (18.4) $6/23$ (18.4) $6/23$ (18.4)   |                 |
| Adjusted rates (b)       22.50       23.81       21.95         Terminal rates (c) $9/40$ (22.5) $10/42$ (23.8) $7/38$ (18.4) $6/23$ (18.4)         Statistical analysis       Peto test $7/38$ (18.4) $6/23$ (18.4) $6/23$ (18.4)         Standard method (d)       P = 1.0000 ?       Prevalence method (d)       P = 0.2050 $6/23$ (18.4) $6/23$ (18.4)         Combined analysis (d)       P = 0.2050 $6/23$ (18.4) $6/23$ (18.4) $6/23$ (18.4)         Cochran-Armitage test (e)       P = 0.2562 $6/23$ (18.4) $6/23$ (18.4) $6/23$ (18.4)   | 22. 0)          |
| Statistical analysis         Peto test         Standard method(d)       P = 1.0000 ?         Prevalence method(d)       P = 0.2050         Combined analysis(d)       P = 0.2562         Cochran-Armitage test(e)       P = 0.8898  | 26.92           |
| Standard method(d) $P = 1.0000$ ?Prevalence method(d) $P = 0.2050$ Combined analysis(d) $P = 0.2562$ Cochran-Armitage test(e) $P = 0.8898$  | 26.1)           |
| Prevalence method(d)P = 0.2050Combined analysis(d)P = 0.2562Cochran-Armitage test(e)P = 0.8898  |                 |
| Combined analysis(d) P = 0.2562<br>Cochran-Armitage test(e) P = 0.8898  |                 |
| Cochran-Armitage test(e) $P = 0.8898$   |                 |
|   |                 |
|   | <del>)</del> 52 |
| SITE : pituitary gland<br>TUMOR : adenoma, adenocarcinoma   |                 |
| Tumor rate  |                 |
| Overall rates(a) 11/50(22.0) 11/50(22.0) 9/50(18.0) 13/50(  | 26.0)           |
| Adjusted rates(b) 22.50 26.19 21.95   | 30. 77          |
| Terminal rates(c)         9/40(22.5)         11/42(26.2)         7/38(18.4)         7/23(           Statistical analysis         Peto test  | 30. 4)          |
| Standard method(d) $P = 0.2496$ Prevalence method(d) $P = 0.1421$   |                 |
| Combined analysis(d) $P = 0.1161$   |                 |
| Cochran-Armitage         test(e)         P = 0.5592           Fisher         Exact         test(e)         P = 0.5952         P = 0.4016         P = 0.4016   | 070             |
| Fisher Exact test(e) $P = 0.5952$ $P = 0.4016$ $P = 0.4016$   | 075             |

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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# STUDY No. : 0342

(HPT360A)

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#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name  | 0 ppm   | 3 ppm  | 10 ppm                                    | 30 ppm   |
|---|---|--|---|--|
|   | SITE : thyroid  |  |   |  |
| ·····   | TUMOR : C-cell adenoma  |  |   |  |
| umor rate<br>Overall rates(a)   | 14/50(28.0)   | 17/50(34.0)  | 15/50( 30.0)                              | 14/50(28.0)                                    |
| Adjusted rates(b)   | 34. 15  | 38.64  | 33. 33                                    | 14/50(28.0)<br>35.90                           |
| Terminal rates(c)   | 13/40(32.5)   | 15/42(35.7)  | 12/38(31.6)                               | 7/23(30.4)                                     |
| tatistical analysis   | 10/10(02.0)   | 10/42( 00.1)   | 12/30( 51.0)                              | 1/23( 30.4)                                    |
| Peto test   |   |  |   |  |
| Standard method(d)  | P =   |  |   |  |
| Prevalence method(d)  | P = 0.4036  |  |   |  |
| Combined analysis(d)  | P =   |  |   |  |
| Cochran-Armitage test(e)  | P = 0.7514  |  |   |  |
| Fisher Exact test(e)  |   | P = 0.3329   | P = 0.5000                                | P = 0.5880                                     |
| Yumor rate<br>Overall rates(a)<br>Adjusted rates(b)<br>Terminal rates(c)<br>Statistical analysis<br>Peto test<br>Standard method(d)<br>Prevalence method(d)<br>Combined analysis(d)<br>Cochran-Armitage test(e)<br>Fisher Exact test(e) | SITE : thyroid<br>TUMOR : follicular ademocarcin<br>0/50( 0.0)<br>0.0<br>0/40( 0.0)<br>P =<br>P = 0.0014**<br>P =<br>P = 0.0073** | DTMA<br>1/50( 2.0)<br>2.38<br>1/42( 2.4)<br>P = 0.5000 | 0/50(0.0)<br>0.0<br>0/38(0.0)<br>P = N.C. | 4/50(8.0)<br>14.29<br>3/23(13.0)<br>P = 0.0587 |
|   | SITE : thyroid<br>TUMOR : C-cell adenoma,C-cell   | carcinoma  |   |  |
| lumor rate<br>Overall rates(a)  | 14/50( 39 0)  | 17/50/ 34 0)   | 10 (50 ( 20 0)                            |  |
| Adjusted rates(b)   | 14/50(28.0)<br>34.15  | 17/50(34.0)<br>38.64                                   | 16/50(32.0)<br>35.90                      | 15/50(30.0)                                    |
| Terminal rates(c)   | 13/40 ( 32, 5)  | 38. 64<br>15/42(35. 7)                                 | 35.90<br>13/38(34.2)                      | 38.46<br>8/23 (34.8)                           |
| Statistical analysis<br>Peto test   | 10, 10( 00, 0)  | 10/ 46 \ 00. 1/  | 10/00 ( 04.2/                             | 0/63 ( 34.0/                                   |
| Standard method(d)  | P =   |  |   |  |
| Prevalence method(d)  | P = 0.3029  |  |   |  |
| Combined analysis(d)  | P =   |  |   |  |
| Cochran-Armitage test(e)  | P = 0.9427  |  |   |  |
| Fisher Exact test(e)  |   | P = 0.3329   | P = 0.4138                                | P = 0.5000                                     |

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name               | 0 ppm                                            | 3 ppm                     | 10 ppm             | 30 ppm               |       |
|--------------------------|--------------------------------------------------|---------------------------|--------------------|----------------------|-------|
|                          | SITE : thyroid                                   |                           |                    |                      | · · · |
| _                        | TUMOR : follicular adenoma,                      | follicular adenocarcinoma |                    |                      |       |
| fumor rate               |                                                  |                           |                    |                      |       |
| Overall rates(a)         | 0/50( 0.0)                                       | 2/50( 4.0)                | 2/50( 4.0)         | 4/50( 8.0)           |       |
| Adjusted rates(b)        | 0.0                                              | 4.76                      | 5.26               | 14. 29               |       |
| Terminal rates(c)        | 0/40( 0.0)                                       | 2/42( 4.8)                | 2/38( 5.3)         | 3/23(13.0)           |       |
| tatistical analysis      |                                                  |                           |                    |                      |       |
| Peto test                | _                                                |                           |                    |                      |       |
| Standard method(d)       | P =                                              |                           |                    |                      |       |
| Prevalence method(d)     | P = 0.0114*                                      |                           |                    |                      |       |
| Combined analysis(d)     | P =                                              |                           |                    |                      |       |
| Cochran-Armitage test(e) | P = 0.0640                                       |                           |                    |                      |       |
| Fisher Exact test(e)     |                                                  | P = 0.2475                | P = 0.2475         | P = 0.0587           |       |
|                          |                                                  |                           |                    |                      | · · · |
|                          | SITE : adrenal gland<br>TUMOR : pheochromocytoma |                           |                    |                      |       |
| lumor rate               | TUMOR : pheochromocytoma                         |                           |                    |                      |       |
| Overall rates(a)         | 5/50(10.0)                                       | 6/50(12.0)                | 4/50( 8.0)         |                      |       |
| Adjusted rates(b)        | 12.50                                            | 14. 29                    | 4/50( 8.0)<br>8.33 | 5/50( 10.0)<br>14.29 |       |
| Terminal rates(c)        | 5/40(12.5)                                       | 6/42(14.3)                | 3/38(7,9)          | 3/23(13.0)           |       |
| Statistical analysis     | 0/40(12.0)                                       | 0/42(14.3)                | 3/30( 1.9)         | 3/23(13.0)           |       |
| Peto test                |                                                  |                           |                    |                      |       |
| Standard method(d)       | P =                                              |                           |                    |                      |       |
| Prevalence method(d)     | P = 0.3886                                       |                           |                    |                      |       |
| Combined analysis(d)     | P =                                              |                           |                    |                      |       |
| Cochran-Armitage test(e) | P = 0.8878                                       |                           |                    |                      |       |
| Fisher Exact test(e)     |                                                  | P = 0.5000                | P = 0.5000         | P = 0.6297           | -     |
|                          |                                                  |                           |                    | 1 0.0257             |       |
|                          | SITE : adrenal gland                             |                           |                    |                      |       |
|                          | TUMOR : pheochromocytoma, ph                     | eochromocytoma:malignant  |                    |                      |       |
| lumor rate               |                                                  | -                         |                    |                      |       |
| Overall rates(a)         | 5/50( 10.0)                                      | 6/50(12.0)                | 5/50(10.0)         | 6/50(12.0)           |       |
| Adjusted rates(b)        | 12.50                                            | 14. 29                    | 8.51               | 17.86                |       |
| Terminal rates(c)        | 5/40(12.5)                                       | 6/42(14.3)                | 3/38( 7.9)         | 3/23(13.0)           |       |
| Statistical analysis     |                                                  |                           |                    |                      |       |
| Peto test                |                                                  |                           |                    |                      |       |
| Standard method(d)       | P = 0.3394                                       |                           |                    |                      |       |
| Prevalence method(d)     | P = 0.2496                                       |                           |                    |                      |       |
| Combined analysis(d)     | P = 0.2543                                       |                           |                    |                      |       |
| Cochran-Armitage test(e) | P = 0.8241                                       |                           |                    |                      |       |
| Fisher Exact test(e)     |                                                  | P = 0,5000                | P = 0.6297         | P = 0,5000           |       |

Tumor rate Overall rates(a)

Adjusted rates(b)

Terminal rates(c)

Statistical analysis Peto test

Standard method(d)

Prevalence method(d)

Combined analysis(d)

Fisher Exact test(e)

Cochran-Armitage test(e)

Group Name

0 ppm

90.91

36/40(90.0)

P = -----

P = -----

P = 0.0159\*

P = 0.0001\*\*

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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3 ppm

#### 30 ppm 10 ppm SITE : testis TUMOR : interstitial cell tumor 41/50(82.0) 37/50(74.0) 44/50( 88.0) 47/50(94.0) 80.95 97.44 97.30 37/38(97.4) 34/42(81.0) 22/23(95.7) P = 0.2348P = 0.2883P = 0.0606

|                          | SITE : mammary gland<br>TUMOR : fibroadenoma |                                       |      |          |      |             |  |
|--------------------------|----------------------------------------------|---------------------------------------|------|----------|------|-------------|--|
| Tumor rate               |                                              |                                       |      |          |      |             |  |
| Overall rates(a)         | 0/50( 0.0)                                   | 0/50(                                 | 0.0) | 0/50(    | 0.0) | 6/50(12.0)  |  |
| Adjusted rates(b)        | 0. 0                                         |                                       | 0.0  |          | 0.0  | 16.67       |  |
| Terminal rates(c)        | 0/40( 0.0)                                   | 0/42(                                 | 0.0) | 0/38(    | 0.0) | 3/23 (13.0) |  |
| Statistical analysis     |                                              |                                       |      |          |      |             |  |
| Peto test                |                                              |                                       |      |          |      |             |  |
| Standard method(d)       | P = 0.0805                                   |                                       |      |          |      |             |  |
| Prevalence method(d)     | P < 0.0001**?                                |                                       |      |          |      |             |  |
| Combined analysis(d)     | P < 0.0001**?                                |                                       |      |          |      |             |  |
| Cochran-Armitage test(e) | P < 0.0001**                                 |                                       |      |          |      |             |  |
| Fisher Exact test(e)     |                                              | P = N.C.                              |      | P = N.C. |      | P = 0.0133* |  |
|                          | SITE : mammary gland                         | · · · · · · · · · · · · · · · · · · · | ,    |          |      |             |  |
|                          | TUMOR : adenoma, fibroadenoma                |                                       |      |          |      |             |  |
| Tumor rate               |                                              |                                       |      |          |      |             |  |
| Overall rates(a)         | 0/50( 0.0)                                   | 0/50(                                 | 0.0) | 0/50(    | 0,0) | 7/50(14.0)  |  |
| Adjusted rates(b)        | 0.0                                          |                                       | 0.0  |          | 0.0  | 20.00       |  |
| Terminal rates(c)        | 0/40( 0.0)                                   | 0/42(                                 | 0.0) | 0/38(    | 0.0) | 4/23(17.4)  |  |

| Statistical analysis     |               |           |           |              |
|--------------------------|---------------|-----------|-----------|--------------|
| Peto test                |               |           |           |              |
| Standard method(d)       | P = 0.0805    |           |           |              |
| Prevalence method(d)     | P < 0.0001**? |           |           |              |
| Combined analysis(d)     | P < 0.0001**? |           |           |              |
| Cochran-Armitage test(e) | P < 0.0001**  |           |           |              |
| Fisher Exact test(e)     |               | P = N. C. | P = N. C. | P = 0.0062** |

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 9

| Group Name               | 0 ppm                | 3 ppm      | 10 ppm       | 30 ppm        |  |
|--------------------------|----------------------|------------|--------------|---------------|--|
|                          | SITE : peritoneum    |            |              |               |  |
|                          | TUMOR : mesothelioma |            |              |               |  |
| lumor rate               |                      |            |              |               |  |
| Overall rates(a)         | 2/50( 4.0)           | 3/50(6.0)  | 12/50(24.0)  | 22/50(44.0)   |  |
| Adjusted rates(b)        | 5.00                 | 4.76       | 25.00        | 32,00         |  |
| Terminal rates(c)        | 2/40(5,0)            | 2/42( 4.8) | 9/38(23.7)   | 7/23 ( 30. 4) |  |
| tatistical analysis      |                      |            | 0,00( 00.1)  | 1720( 00. 17  |  |
| Peto test                |                      |            |              |               |  |
| Standard method(d)       | P < 0.0001**         |            |              |               |  |
| Prevalence method(d)     | P = 0.0003**         |            |              |               |  |
| Combined analysis(d)     | P < 0.0001**         |            |              |               |  |
| Cochran-Armitage test(e) | P < 0.0001***        |            |              |               |  |
| Fisher Exact test(e)     |                      | P = 0.5000 | P = 0.0038** | P < 0.0001**  |  |

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

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

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

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

APPENDIX M 2

# NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL

ANALYSIS, RAT : FEMALE

(2-YEAR STUDY)

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                   | 0 ppm                             | 3 ppm              | 10 ppm            | 30 ppm                         |  |
|----------------------------------------------|-----------------------------------|--------------------|-------------------|--------------------------------|--|
|                                              | SITE : nasal cavity               |                    |                   |                                |  |
|                                              | TUMOR : adenoma                   |                    |                   |                                |  |
| umor rate<br>Overall rates(a)                |                                   |                    |                   |                                |  |
| Adjusted rates(b)                            | 0/50( 0.0)<br>0.0                 | 0/50( 0.0)         | 4/49( 8.2)        | 8/50(16.0)                     |  |
| Terminal rates(c)                            | 0/41 ( 0.0)                       | 0.0<br>0/38( 0.0)  | 9.52              | 21.21                          |  |
| tatistical analysis<br>Peto test             | 0,41( 0.0)                        | 0/38( 0.0)         | 3/39(7.7)         | 6/32(18.8)                     |  |
| Standard method(d)                           | P =                               |                    |                   |                                |  |
| Prevalence method(d)                         | P = 0.0001**                      |                    |                   |                                |  |
| Combined analysis(d)                         | P =                               |                    |                   |                                |  |
| Cochran-Armitage test(e)                     | P = 0.0001**                      |                    |                   |                                |  |
| Fisher Exact test(e)                         |                                   | P = N. C.          | P = 0.0563        | P = 0.0029**                   |  |
|                                              | SITE : nasal cavity               |                    |                   |                                |  |
|                                              | TUMOR : adenoma, adenocarcinoma   |                    |                   |                                |  |
| umor rate                                    |                                   |                    |                   |                                |  |
| Overall rates(a)                             | 0/50(0.0)                         | 0/50( 0.0)         | 4/49( 8.2)        | 10/50(20.0)                    |  |
| Adjusted rates(b)                            | 0.0                               | 0.0                | 9.52              | 21.43                          |  |
| Terminal rates(c)                            | 0/41( 0.0)                        | 0/38( 0.0)         | 3/39(7.7)         | 6/32(18.8)                     |  |
| tatistical analysis                          |                                   |                    |                   |                                |  |
| Peto test                                    |                                   |                    |                   |                                |  |
| Standard method(d)                           | P = 0.1407                        |                    |                   |                                |  |
| Prevalence method(d)<br>Combined analysis(d) | P < 0.0001**                      |                    |                   |                                |  |
| Cochran-Armitage test(e)                     | P < 0.0001***<br>P < 0.0001**     |                    |                   |                                |  |
| Fisher Exact test(e)                         | 1 ( 0.0001                        | P = N, C.          | P = 0.0563        | $\mathbf{D} = 0 0 0 0 0 0 0 0$ |  |
|                                              |                                   | I - N. C.          | r - 0.0003        | P = 0.0006**                   |  |
|                                              | SITE : spleen                     |                    |                   |                                |  |
| umor rate                                    | TUMOR : mononuclear cell leukemia |                    |                   |                                |  |
| umor rate<br>Overall rates(a)                | 2/50/ 6 0)                        |                    | 1/10/ 0.0         |                                |  |
| Adjusted rates(b)                            | 3/50( 6.0)<br>4.88                | 3/50( 6.0)<br>2.63 | 1/49(2.0)         | 8/50(16.0)                     |  |
| Terminal rates(c)                            | 4.88<br>2/41( 4.9)                | 2.63<br>1/38(2.6)  | 0.0<br>0/39( 0.0) | 12.50<br>4/32(12.5)            |  |
| tatistical analysis<br>Peto test             | 0/11( 1.0)                        | 1/30( 2.0)         | 0/39( 0.0)        | 4/32(12.3)                     |  |
| Standard method(d)                           | P = 0.0599                        |                    |                   |                                |  |
| Prevalence method(d)                         | P = 0.0398*                       |                    |                   |                                |  |
| Combined analysis(d)                         | P = 0.0097**                      |                    |                   |                                |  |
| Cochran-Armitage test(e)                     | P = 0.0252*                       |                    |                   |                                |  |
| Fisher Exact test(e)                         |                                   | P = 0.6611         | P = 0.3163        | P = 0.0999                     |  |

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                       | mqq O                           | 3 ppm                      | 10 ppm                | 30 ppm                                |  |
|--------------------------------------------------|---------------------------------|----------------------------|-----------------------|---------------------------------------|--|
|                                                  | SITE : pituitary gland          |                            |                       |                                       |  |
|                                                  | TUMOR : adenoma                 |                            |                       |                                       |  |
| `umor rate<br>Overall rates(a)                   | 10/50/ 00 0)                    | 10/50/ 04 0)               |                       | 10 (50 ( 00 0)                        |  |
| Adjusted rates(b)                                | 13/50(26.0)<br>26.83            | 12/50(24.0)<br>23.68       | 15/49( 30.6)<br>33.33 | 10/50(20.0)<br>21.88                  |  |
| Terminal rates(c)                                | 11/41(26.8)                     | 9/38(23.7)                 | 13/39(33,3)           | 7/32(21.9)                            |  |
| Statistical analysis<br>Peto test                | 11/41(20.0)                     | <del>9</del> / 90 ( 20. 1) | 13/39 ( 33. 3)        | 1/32(21.9)                            |  |
| Standard method(d)                               | P = 0.7714                      |                            |                       |                                       |  |
| Prevalence method(d)                             | P = 0.5165                      |                            |                       |                                       |  |
| Combined analysis(d)                             | P = 0.6454                      |                            |                       |                                       |  |
| Cochran-Armitage test(e)                         | P = 0.4711                      |                            |                       |                                       |  |
| Fisher Exact test(e)                             |                                 | P = 0.5000                 | P = 0.3874            | P = 0.3176                            |  |
|                                                  | SITE : pituitary gland          |                            |                       | · · · · · · · · · · · · · · · · · · · |  |
|                                                  | TUMOR : adenocarcinoma          |                            |                       |                                       |  |
| lumor rate                                       |                                 |                            |                       |                                       |  |
| Overall rates(a)                                 | 2/50( 4.0)                      | 4/50( 8.0)                 | 1/49(2.0)             | 1/50(2.0)                             |  |
| Adjusted rates(b)                                | 2.44                            | 7.89                       | 2.56                  | 3. 13                                 |  |
| Terminal rates(c)                                | 1/41 ( 2.4)                     | 3/38(7.9)                  | 1/39( 2.6)            | 1/32( 3.1)                            |  |
| Statistical analysis                             |                                 |                            |                       |                                       |  |
| Peto test                                        |                                 |                            |                       |                                       |  |
| Standard method(d)                               | P = 0.8699                      |                            |                       |                                       |  |
| Prevalence method(d)                             | P = 0.6075                      |                            |                       |                                       |  |
| Combined analysis(d)<br>Cochran-Armitage test(e) | P = 0.7980<br>P = 0.2947        |                            |                       |                                       |  |
| Fisher Exact test(e)                             | 1 - 0.2547                      | P = 0.3389                 | P = 0.5077            | P = 0.5000                            |  |
|                                                  |                                 | 1 - 0.000                  | r = 0.0000            | r = 0.5000                            |  |
|                                                  | SITE : pituitary gland          |                            |                       |                                       |  |
| _                                                | TUMOR : adenoma, adenocarcinoma |                            |                       |                                       |  |
| Tumor rate                                       |                                 |                            |                       |                                       |  |
| Overall rates (a)                                | 15/50 ( 30. 0)                  | 16/50(32.0)                | 16/49 ( 32. 7)        | 11/50(22.0)                           |  |
| Adjusted rates(b)<br>Terminal rates(c)           | 29.27<br>12/41(29.3)            | 31.58<br>12/38(31.6)       | 35.90                 | 25.00                                 |  |
| Statistical analysis                             | 12/41( 29.3)                    | 12/38( 31.6)               | 14/39(35.9)           | 8/32(25.0)                            |  |
| Peto test                                        |                                 |                            |                       |                                       |  |
| Standard method(d)                               | P = 0.8905                      |                            |                       |                                       |  |
| Prevalence method(d)                             | P = 0.5960                      |                            |                       |                                       |  |
| Combined analysis(d)                             | P = 0.7811                      |                            |                       |                                       |  |
| Cochran-Armitage test(e)                         | P = 0.2539                      |                            |                       |                                       |  |
| Fisher Exact test(e)                             |                                 | P = 0.5000                 | P = 0.4729            | P = 0.2472                            |  |

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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|--------------------------------------------------|-----------------------------------|---------------------|-------------------------|---------------------|--------------|
| Group Name                                       | 0 ppm                             | 3 ppm               | 10 ppm                  | 30 ppm              |              |
|                                                  | SITE : thyroid                    |                     |                         |                     |              |
| _                                                | TUMOR : C-cell adenoma            |                     |                         |                     |              |
| Tumor rate<br>Overall rates(a)                   | 9/50(18.0)                        |                     |                         |                     |              |
| Adjusted rates(b)                                | 21.95                             | 5/50(10.0)<br>11.36 | 8/49 ( 16. 3)<br>20. 00 | 7/50(14.0)<br>16.67 |              |
| Terminal rates(c)                                | 9/41 ( 22. 0)                     | 4/38(10.5)          | 7/39(17.9)              | 5/32(15.6)          |              |
| Statistical analysis                             |                                   |                     | () 00 ( 1110)           | 0,02(10.0)          |              |
| Peto test                                        |                                   |                     |                         |                     |              |
| Standard method(d)                               | P =                               |                     |                         |                     |              |
| Prevalence method(d)                             | P = 0.4560                        |                     |                         |                     |              |
| Combined analysis(d)<br>Cochran-Armitage test(e) | P =P = 0.9064                     |                     |                         |                     |              |
| Fisher Exact test(e)                             | 1 - 0.3004                        | P = 0.1940          | P = 0.5184              | P = 0.3929          |              |
|                                                  |                                   |                     | 1 - 0.0104              | 1 - 0.3929          |              |
|                                                  | SITE : thyroid                    |                     |                         |                     |              |
|                                                  | TUMOR : C-cell adenoma, C-cell of | rarcinoma           |                         |                     |              |
| Tumor rate                                       |                                   |                     |                         |                     |              |
| Overall rates(a)                                 | 9/50(18.0)                        | 5/50(10.0)          | 8/49(16.3)              | 8/50(16.0)          |              |
| Adjusted rates(b)                                | 21.95                             | 11.36               | 20.00                   | 19.44               |              |
| Terminal rates(c)                                | 9/41(22.0)                        | 4/38(10.5)          | 7/39(17.9)              | 6/32(18.8)          |              |
| Statistical analysis<br>Peto test                |                                   |                     |                         |                     |              |
| Standard method(d)                               | P =                               |                     |                         |                     |              |
| Prevalence method(d)                             | P = 0.3250                        |                     |                         |                     |              |
| Combined analysis(d)                             | P =                               |                     |                         |                     |              |
| Cochran-Armitage test(e)                         | P = 0.8342                        |                     |                         |                     |              |
| Fisher Exact test(e)                             |                                   | P = 0.1940          | P = 0.5184              | P = 0.5000          |              |
|                                                  | SITE : adrenal gland              |                     |                         |                     |              |
|                                                  | TUMOR : pheochromocytoma          |                     |                         |                     |              |
| Tumor rate                                       |                                   |                     |                         |                     |              |
| Overall rates(a)                                 | 3/50( 6.0)                        | 3/50( 6.0)          | 1/49( 2.0)              | 0/50( 0.0)          |              |
| Adjusted rates(b)                                | 7.32                              | 7.89                | 2.56                    | 0.0                 |              |
| Terminal rates(c)<br>Statistical analysis        | 3/41(7.3)                         | 3/38(7.9)           | 1/39( 2.6)              | 0/32( 0.0)          |              |
| Peto test                                        |                                   |                     |                         |                     |              |
| Standard method(d)                               | P =                               |                     |                         |                     |              |
| Prevalence method(d)                             | P = 0.9717                        |                     |                         |                     |              |
| Combined analysis(d)                             | P =                               |                     |                         |                     |              |
| Cochran-Armitage test(e)                         | P = 0.0647                        |                     |                         |                     |              |
| Fisher Exact test(e)                             |                                   | P = 0.6611          | P = 0.3163              | P = 0.1212          |              |

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                       | 0 ppm                                           | 3 ppm                                | 10 ppm      | 30 ppm      |
|--------------------------------------------------|-------------------------------------------------|--------------------------------------|-------------|-------------|
|                                                  | SITE : adrenal gland                            |                                      |             |             |
| Tumor rate                                       | TUMOR : pheochromocytoma, pheod                 | chromocytoma:malignant               |             |             |
| Overall rates(a)                                 |                                                 |                                      |             |             |
| Adjusted rates(b)                                | 3/50 ( 6.0)                                     | 5/50(10.0)                           | 1/49( 2.0)  | 0/50( 0.0)  |
| Terminal rates(c)                                | 7.32<br>3/41(7.3)                               | 10.53                                | 2.56        | 0.0         |
| Statistical analysis<br>Peto test                | 3/41( 1.3)                                      | 4/38(10.5)                           | 1/39( 2.6)  | 0/32( 0.0)  |
| Standard method(d)                               | P = 0,5280                                      |                                      |             |             |
| Prevalence method(d)                             | P = 0.9796                                      |                                      |             |             |
| Combined analysis(d)                             | P = 0.9855                                      |                                      |             |             |
| Cochran-Armitage test(e)                         | P = 0.0367*                                     |                                      |             |             |
| Fisher Exact test(e)                             |                                                 | P = 0.3575                           | P = 0.3163  | P = 0.1212  |
| Tumor rate                                       | SITE : uterus<br>TUMOR : endometrial stromal po | olyp                                 |             |             |
| Overall rates(a)                                 | 6/50(12.0)                                      | 11/50(22.0)                          | 11/49(22.4) | 13/50(26.0) |
| Adjusted rates(b)                                | 14. 63                                          | 26.19                                | 26.83       | 34. 29      |
| Terminal rates(c)                                | 6/41(14.6)                                      | 9/38(23.7)                           | 9/39(23.1)  | 10/32(31.3) |
| Statistical analysis                             |                                                 |                                      |             |             |
| Peto test                                        | _                                               |                                      |             |             |
| Standard method(d)                               | P =                                             |                                      |             |             |
| Prevalence method(d)                             | P = 0.0471*                                     |                                      |             |             |
| Combined analysis(d)                             | P =                                             |                                      |             |             |
| Cochran-Armitage test(e)<br>Fisher Exact test(e) | P = 0.1685                                      |                                      |             |             |
| risher Exact test(e)                             |                                                 | P = 0.1434                           | P = 0.1330  | P = 0.0624  |
|                                                  | SITE : uterus<br>TUMOR : adenocarcinoma         |                                      |             |             |
| Tumor rate                                       |                                                 |                                      |             |             |
| Overall rates(a)                                 | 0/50( 0.0)                                      | 0/50( 0.0)                           | 3/49(6.1)   | 0/50(0.0)   |
| Adjusted rates(b)                                | 0.0                                             | 0.0                                  | 5.13        | 0.0         |
| Terminal rates(c)                                | 0/41( 0.0)                                      | 0/38( 0.0)                           | 2/39(5.1)   | 0/32( 0.0)  |
| Statistical analysis                             |                                                 |                                      |             |             |
| Peto test                                        |                                                 |                                      |             |             |
| Standard method(d)                               | P = 0.3409                                      |                                      |             |             |
| Prevalence method(d)                             | P = 0.4191                                      |                                      |             |             |
| Combined analysis(d)                             | P = 0.4388                                      |                                      |             |             |
| Cochran-Armitage test(e)<br>Fisher Exact test(e) | P = 0.9106                                      | $\mathbf{D} = \mathbf{N} \mathbf{Q}$ | <b>D</b>    |             |
| TOUCT EVACT (620(6)                              |                                                 | P = N. C.                            | P = 0.1175  | P = N. C.   |

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#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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PAGE: 14

| Group Name                                                                                                  | mqq 0                                                                       | 3 ppm                          | 10 ppm                           | 30 ppm                             |
|-------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|--------------------------------|----------------------------------|------------------------------------|
|                                                                                                             | SITE : uterus                                                               |                                |                                  |                                    |
|                                                                                                             | TUMOR : endometrial stromal sam                                             | coma                           |                                  |                                    |
| umor rate                                                                                                   |                                                                             |                                |                                  |                                    |
| Overall rates(a)                                                                                            | 1/50( 2.0)                                                                  | 4/50( 8.0)                     | 4/49( 8.2)                       | 7/50(14.0)                         |
| Adjusted rates(b)<br>Terminal rates(c)                                                                      | 0.0                                                                         | 5. 26                          | 2.56                             | 3. 13                              |
| tatistical analysis                                                                                         | 0/41( 0.0)                                                                  | 2/38( 5.3)                     | 1/39( 2.6)                       | 1/32( 3.1)                         |
| Peto test                                                                                                   |                                                                             |                                |                                  |                                    |
| Standard method(d)                                                                                          | P = 0.0152*                                                                 |                                |                                  |                                    |
| Prevalence method(d)                                                                                        | P = 0.3505                                                                  |                                |                                  |                                    |
| Combined analysis(d)                                                                                        | P = 0.0201*                                                                 |                                |                                  |                                    |
| Cochran-Armitage test(e)                                                                                    | P = 0.0454*                                                                 |                                |                                  |                                    |
| Fisher Exact test(e)                                                                                        |                                                                             | P = 0.1811                     | P = 0.1748                       | P = 0.0297*                        |
| umor rate<br>Overall rates(a)<br>Adjusted rates(b)<br>Terminal rates(c)<br>tatistical analysis<br>Peto test | SITE : mammary gland<br>TUMOR : adenoma<br>2/50( 4.0)<br>4.26<br>1/41( 2.4) | 1/50(2.0)<br>2.56<br>0/38(0.0) | 3/49( 6.1)<br>7.14<br>2/39( 5.1) | 2/50 ( 4.0)<br>6.25<br>2/32 ( 6.3) |
| Standard method(d)<br>Prevalence method(d)<br>Combined analysis(d)<br>Cochran-Armitage test(e)              | P =<br>P = 0.3835<br>P =<br>P = 0.8301                                      |                                |                                  |                                    |
| Fisher Exact test(e)                                                                                        |                                                                             | P = 0.5000                     | P = 0.4903                       | P = 0.6913                         |
| umor rate                                                                                                   | SITE : mammary gland<br>TUMOR : fibroadenoma                                |                                |                                  |                                    |
| Overall rates(a)                                                                                            | 8/50(16.0)                                                                  | 6/50(12,0)                     | 10/10/ 00 7                      |                                    |
| Adjusted rates(b)                                                                                           | 19.51                                                                       | 15.79                          | 18/49(36.7)                      | 17/50(34.0)                        |
| Terminal rates(c)                                                                                           | 8/41 ( 19.5)                                                                | 6/38(15.8)                     | 38.46<br>15/39(38.5)             | 43.75                              |
| tatistical analysis<br>Peto test                                                                            | 0, 11 ( 10 0)                                                               | 0/00(10.0)                     | 10/ 99( 90. 9)                   | 14/32(43.8)                        |
| Standard method(d)                                                                                          | P =                                                                         |                                |                                  |                                    |
| Prevalence method(d)                                                                                        | P = 0.0014**                                                                |                                |                                  |                                    |
| Combined analysis(d)                                                                                        | P =                                                                         |                                |                                  |                                    |
| Cochran-Armitage test(e)                                                                                    | P = 0.0110*                                                                 |                                |                                  |                                    |
| Fisher Exact test(e)                                                                                        |                                                                             | P = 0.3871                     | P = 0.0167*                      | P = 0,0317*                        |

(HPT360A)

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 15

|                                   |                                                                                  |                                             | 30 ppm                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|-----------------------------------|----------------------------------------------------------------------------------|---------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SITE : mammary gland              |                                                                                  |                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| UMOR : adenoma, fibroadenoma      |                                                                                  |                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|                                   |                                                                                  |                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|                                   | 7/50(14.0)                                                                       | 20/49(40.8)                                 | 17/50(34,0)                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|                                   | 17.95                                                                            | 42.55                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| 9/41 (22.0)                       | 6/38(15.8)                                                                       | 16/39(41.0)                                 | 14/32(43.8)                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|                                   |                                                                                  |                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| _                                 |                                                                                  |                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
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| •                                 |                                                                                  |                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| P = 0.0409*                       |                                                                                  |                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|                                   | P = 0.2977                                                                       | P = 0.0205*                                 | P = 0.0880                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| TTT:                              |                                                                                  |                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|                                   |                                                                                  |                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| umuk · adenoma, i i broadenoma, a | denocarcinoma                                                                    |                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| 10/50( 20 0)                      |                                                                                  |                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|                                   |                                                                                  |                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|                                   |                                                                                  |                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| 3/11(22.0)                        | (/38(18.4)                                                                       | 17/39(43.6)                                 | 15/32(46.9)                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|                                   |                                                                                  |                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| P = 0.1346                        |                                                                                  |                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|                                   |                                                                                  |                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| P = 0.0038 * *                    |                                                                                  |                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| P = 0.0164*                       |                                                                                  |                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|                                   | P = 0.3976                                                                       | P = 0.0123*                                 | P = 0.0385*                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|                                   | 10/50(20.0)<br>21.95<br>9/41(22.0)<br>P = 0.1346<br>P = 0.0073**<br>P = 0.0038** | 21.95 17.95<br>9/41(22.0) 6/38(15.8)<br>P = | $\begin{array}{c} 21.95 & 17.95 & 42.55 \\ 9/41(22.0) & 6/38(15.8) & 16/39(41.0) \end{array}$ $P = \\ P = \\ P = 0.0112* \\ P = 0.0409* & P = 0.2977 & P = 0.0205* \end{array}$ $ITE : mammary gland \\ IMOR : adenoma, fibroadenoma, adenocarcinoma \\ 10/50(20.0) & 8/50(16.0) & 21/49(42.9) \\ 21.95 & 20.51 & 44.68 \\ 9/41(22.0) & 7/38(18.4) & 17/39(43.6) \end{array}$ $P = 0.1346 \\ P = 0.0073** \\ P = 0.0164* & P = 0.0164* \\ \end{array}$ | $\begin{array}{c} 21.95 \\ 9/41(22.0) \\ P = \\ P = 0.0112* \\ P = \\ P = 0.0409* \\ \hline P = \\ P = 0.0409* \\ \hline P = 0.2977 \\ P = 0.0205* \\ P = 0.0205* \\ P = 0.0880 \\ \hline P = 0.08$ |

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

----- : There is no data which should be statistical analysis. Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$ 

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

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APPENDIX N 1

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY

RAT : MALE : ALL ANIMALS

(2-YEAR STUDY)

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

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| )rgan         |                             | o Name 0 ppm<br>of Animals on Study 50 | 3 ppm<br>50 | 10 ppm<br>50 | 30 ppm<br>50 |
|---------------|-----------------------------|----------------------------------------|-------------|--------------|--------------|
| Respiratory   | system)                     |                                        |             |              |              |
| asal cavit    |                             | <50>                                   | <50>        | <50>         | <50>         |
|               | leukemic cell infiltration  | 1                                      | 0           | 0            | 0            |
| lung          |                             | <50>                                   | <50>        | <50>         | <50>         |
|               | leukemic cell infiltration  | 6                                      | 1           | 3            | 2            |
|               | metastasis:thyroid tumor    | 0                                      | . 0         | 0            | 1            |
|               | metastasis:peritoneum tumor | 0                                      | 0           | 0            | 1            |
|               |                             |                                        |             |              |              |
| Hematopoieti  | c system)                   |                                        |             |              |              |
| one marrow    |                             | <50>                                   | <50>        | <50>         | <50>         |
| ۰.            | leukemic cell infiltration  | 5                                      | 0           | 2            | 0            |
| ymph node     | leukemic cell infiltration  | <50><br>3                              | <50><br>0   | <50><br>0    | <50><br>0    |
|               | metastasis:peritoneum tumor | 0                                      | 0           | 0            | 1            |
|               | metastasis.peritoneum tumor | 0                                      | Ŭ           | U            | 1            |
| {Circulatory  | system)                     |                                        |             |              |              |
| heart         |                             | <50>                                   | <50>        | <50>         | <50>         |
|               | leukemic cell infiltration  | 2                                      | 0           | 0            | 0            |
| {Digestive sy | retom)                      |                                        |             |              |              |
|               | () Lett)                    |                                        |             |              |              |
| tongue        | leukemic cell infiltration  | <50><br>0                              | <50><br>0   | <50><br>1    | <50><br>0    |
| salivary gl   |                             | <50>                                   | <50>        | <50>         | <50>         |
| seriveri Ri   | leukemic cell infiltration  | 0                                      | 0           | 1            | 0            |

(JPT150)

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

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|             |                             | Group Name              | 0 ppm     | 3 ppm     | 10 ppm    | 30 ppm    |
|-------------|-----------------------------|-------------------------|-----------|-----------|-----------|-----------|
| an          | Findings                    | No. of Animals on Study | 50        | 50        | 50        | 50        |
| estive sys  | tem}                        |                         |           |           |           |           |
|             |                             |                         |           |           |           |           |
| lvary gl    | metastasis:subcutis tumor   |                         | <50><br>0 | <50><br>0 | <50><br>1 | <50><br>1 |
| mach        | leukemic cell infiltration  |                         | <50><br>2 | <50><br>0 | <50><br>0 | <50><br>0 |
|             | metastasis:peritoneum tumor |                         | 0         | 0         | 0         | 1         |
| all intes   | leukemic cell infiltration  |                         | <50><br>1 | <50><br>0 | <50><br>0 | <50><br>0 |
| rge intes   | leukemic cell infiltration  |                         | <50><br>1 | <50><br>0 | <50><br>0 | <50><br>0 |
|             | metastasis:peritoneum tumor |                         | 0         | 0         | 0         | 1         |
| er          | leukemic cell infiltration  |                         | <50><br>7 | <50><br>1 | <50><br>3 | <50><br>4 |
| creas       | leukemic cell infiltration  |                         | <50><br>3 | <49><br>0 | <50><br>1 | <50><br>0 |
|             | metastasis:peritoneum tumor |                         | 0         | 0         | 0         | 1         |
| inary syst  | em)                         |                         |           | •         |           |           |
| dney        | leukemic cell infiltration  |                         | <50><br>1 | <50><br>1 | <50><br>0 | <50><br>1 |
| in bladd    | leukemic cell infiltration  |                         | <50><br>2 | <50><br>0 | <50><br>0 | <50><br>0 |
| ndocrine sy | stem)                       |                         |           |           |           |           |
| renal       | leukemic cell infiltration  |                         | <50><br>1 | <50><br>0 | <50><br>0 | <50><br>0 |

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

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| SEX :         | : MALE                                                                  |                                       |             |             |              | PAGE :       |
|---------------|-------------------------------------------------------------------------|---------------------------------------|-------------|-------------|--------------|--------------|
| Organ         | Findings                                                                | Group Name<br>No. of Animals on Study | 0 ppm<br>50 | 3 ppm<br>50 | 10 ppm<br>50 | 30 ppm<br>50 |
| {Reproductive | e system)                                                               |                                       |             |             |              |              |
| prostate      | leukemic cell infiltration                                              |                                       | <50><br>2   | <50><br>0   | <50><br>0    | <50><br>0    |
| {Nervous sys  | tem)                                                                    |                                       |             |             |              |              |
| brain         | leukemic cell infiltration                                              |                                       | <50><br>3   | <50><br>1   | <50><br>2    | <50><br>1    |
|               | metastasis:pituitary tumor                                              |                                       | 0           | 1           | 0            | 2            |
| spinal cord   | leukemic cell infiltration                                              |                                       | <50><br>2   | <50><br>1   | <50><br>1    | <50><br>0    |
| {Body caviti  | es)                                                                     |                                       |             |             |              |              |
| pleura        | metastasis:peritoneum tumor                                             |                                       | <50><br>0   | <50><br>0   | <50><br>0    | <50><br>2    |
|               | metastasis:retroperitoneum tumor                                        |                                       | 0           | 0           | 0            | 1            |
| <a>b</a>      | a : Number of animals examined at the b : Number of animals with lesion | site                                  |             |             |              |              |
| (JPT150)      |                                                                         |                                       |             |             |              | BAIS         |

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APPENDIX N 2

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY

RAT : MALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

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

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|                |                                                                              |                                       |             |            |              | 1102 .       |
|----------------|------------------------------------------------------------------------------|---------------------------------------|-------------|------------|--------------|--------------|
| Drgan          | Findings                                                                     | Group Name<br>No. of Animals on Study | 0 ppm<br>10 | 3 ppm<br>8 | 10 ppm<br>12 | 30 ppm<br>27 |
|                |                                                                              |                                       |             |            | <u></u>      |              |
| {Respiratory s | system)                                                                      |                                       |             |            |              |              |
| nasal cavit    | leukemic cell infiltration                                                   |                                       | <10><br>1   | < 8><br>0  | <12><br>0    | <27><br>0    |
| lung           | leukemic cell infiltration                                                   |                                       | <10><br>5   | < 8><br>1  | <12><br>3    | <27><br>2    |
|                | metastasis:peritoneum tumor                                                  |                                       | 0           | 0          | 0            | 1            |
| {Hematopoietic | c system)                                                                    |                                       |             |            |              |              |
| bone marrow    | leukemic cell infiltration                                                   |                                       | <10><br>5   | < 8><br>0  | <12><br>2    | <27><br>0    |
| lymph node     | leukemic cell infiltration                                                   |                                       | <10><br>3   | < 8><br>0  | <12><br>0    | <27><br>0    |
|                | metastasis:peritoneum tumor                                                  |                                       | 0           | 0          | 0            | 1            |
| {Circulatory : | system)                                                                      |                                       |             |            |              |              |
| heart          | leukemic cell infiltration                                                   |                                       | <10><br>2   | < 8><br>0  | <12><br>0    | <27><br>0    |
| {Digestive sys | stem)                                                                        |                                       |             |            |              |              |
| tongue         | leukemic cell infiltration                                                   |                                       | <10><br>0   | < 8><br>0  | <12><br>1    | <27><br>0    |
| salivary gl    | leukemic cell infiltration                                                   |                                       | <10><br>0   | < 8><br>0  | <12><br>1    | <27><br>0    |
|                | metastasis:subcutis tumor                                                    |                                       | 0           | 0          | 0            | 1            |
| <a>b</a>       | a : Number of animals examined at the s<br>b : Number of animals with lesion | site                                  | ******      |            |              |              |

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

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| rgan             | Findings                                                                   | Group Name 0 ppm<br>No. of Animals on Study 10 | 3 ppm<br>8                            | 10 ppm<br>12 | 30 ppm<br>27 |
|------------------|----------------------------------------------------------------------------|------------------------------------------------|---------------------------------------|--------------|--------------|
| )<br>igestive sy | stem)                                                                      |                                                |                                       |              |              |
| tomach           | leukemic cell infiltration                                                 | <10><br>2                                      | < 8><br>0                             | <12><br>0    | <27><br>0    |
|                  | metastasis:peritoneum tumor                                                | 0                                              | 0                                     | 0            | 1            |
| mall intes       | leukemic cell infiltration                                                 | <10><br>1                                      | < 8><br>0                             | <12><br>0    | <27><br>0    |
| arge intes       | leukemic cell infiltration                                                 | <10><br>1                                      | < 8><br>0                             | <12><br>0    | <27><br>0    |
|                  | metastasis:peritoneum tumor                                                | 0                                              | 0                                     | 0            | 1            |
| iver             | leukemic cell infiltration                                                 | <10><br>5                                      | < 8><br>1                             | <12><br>3    | <27><br>2    |
| ancreas          | leukemic cell infiltration                                                 | <10><br>3                                      | < 8><br>0                             | <12><br>1    | <27><br>0    |
|                  | metastasis:peritoneum tumor                                                | 0                                              | 0                                     | 0            | 1            |
| Urinary syst     | em}                                                                        |                                                |                                       |              |              |
| idney            | leukemic cell infiltration                                                 | <10><br>1                                      | < 8><br>1                             | <12><br>0    | <27><br>0    |
| rin bladd        | leukemic cell infiltration                                                 | <10><br>2                                      | < 8><br>0                             | <12><br>0    | <27><br>0    |
| Endocrine sy     | stem)                                                                      |                                                |                                       |              |              |
| drenal           | leukemic cell infiltration                                                 | <10><br>1                                      | < 8><br>0                             | <12><br>0    | <27><br>0    |
| (a)<br>b         | a : Number of animals examined at the<br>b : Number of animals with lesion | site                                           | · · · · · · · · · · · · · · · · · · · |              |              |

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

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| SEX          | : MALE                                                                       |                                       |             |            |              | PAGE :       |
|--------------|------------------------------------------------------------------------------|---------------------------------------|-------------|------------|--------------|--------------|
| Organ        | Findings                                                                     | Group Name<br>No. of Animals on Study | 0 ppm<br>10 | 3 ppm<br>8 | 10 ppm<br>12 | 30 ppm<br>27 |
| {Reproductiv | 'e system}                                                                   |                                       |             |            |              |              |
| prostate     | leukemic cell infiltration                                                   |                                       | <10><br>2   | < 8><br>0  | <12><br>0    | <27><br>0    |
| {Nervous sys | stem}                                                                        |                                       |             |            |              |              |
| brain        | leukemic cell infiltration                                                   |                                       | <10><br>3   | < 8><br>1  | <12><br>2    | <27><br>1    |
|              | metastasis:pituitary tumor                                                   |                                       | 0           | 0          | 0            | 1            |
| spinal cord  | leukemic cell infiltration                                                   |                                       | <10><br>2   | < 8><br>1  | <12><br>1    | <27><br>0    |
| {Body caviti | ies)                                                                         |                                       |             |            |              |              |
| pleura       | metastasis:peritoneum tumor                                                  |                                       | <10><br>0   | < 8><br>0  | <12><br>0    | <27><br>2    |
|              | metastasis:retroperitoneum tumor                                             |                                       | 0           | 0          | 0            | 1            |
| < a ><br>b   | a : Number of animals examined at the s<br>b : Number of animals with lesion | site                                  |             | - · · · ·  |              |              |
| (JPT150)     |                                                                              |                                       |             |            |              | BAI          |

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APPENDIX N 3

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY

RAT : MALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

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

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| SEX          | : MALE                                                                                                                                                                                              |                                       |             |                      |              | PAGE :       |
|--------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------|-------------|----------------------|--------------|--------------|
| Organ        | Findings                                                                                                                                                                                            | Group Name<br>No. of Animals on Study | 0 ppm<br>40 | 3 ppm<br>42          | 10 ppm<br>38 | 30 ppm<br>23 |
| {Respirator; | y system}                                                                                                                                                                                           |                                       |             |                      |              |              |
| lung         | leukemic cell infiltration                                                                                                                                                                          |                                       | <40><br>1   | <42><br>0            | <38><br>0    | <23><br>0    |
|              | metastasis:thyroid tumor                                                                                                                                                                            |                                       | 0           | 0                    | 0            | 1            |
| {Digestive   | system}                                                                                                                                                                                             |                                       |             |                      |              |              |
| salivary gl  | metastasis:subcutis tumor                                                                                                                                                                           |                                       | <40><br>0   | <42><br>0            | <38><br>1    | <23><br>0    |
| liver        | leukemic cell infiltration                                                                                                                                                                          |                                       | <40><br>2   | <42><br>0            | <38><br>0    | <23><br>2    |
| {Urinary sy  | rstem)                                                                                                                                                                                              |                                       |             |                      |              |              |
| kidney       | leukemic cell infiltration                                                                                                                                                                          |                                       | <40><br>0   | <42><br>0            | <38><br>0    | <23><br>1    |
| {Nervous sy  | /stem}                                                                                                                                                                                              |                                       |             |                      |              |              |
| brain        | metastasis:pituitary tumor                                                                                                                                                                          |                                       | <40><br>0   | < <b>42&gt;</b><br>1 | <38><br>0    | <23><br>1    |
| < a ><br>b   | a : Number of animals examined at the s<br>b : Number of animals with lesion                                                                                                                        | site                                  |             |                      |              |              |
| (101100)     | metastasis:subcutis tumor001r(40)(42)(38)leukemic cell infiltration20nary system)(40)(42)(38)eyleukemic cell infiltration00vous system)000vous system)(40)(42)(38)nmetastasis:pituitary tumor010101 |                                       |             |                      | B            |              |

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APPENDIX N 4

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY

RAT : FEMALE: ALL ANIMALS

(2-YEAR STUDY)

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

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| rgan        | Findings                   | Group Name<br>No. of Animals on Study | 0 ppm<br>50 | 3 ppm<br>50 | 10 ppm<br>49 | 30 ppm<br>50 |
|-------------|----------------------------|---------------------------------------|-------------|-------------|--------------|--------------|
|             |                            |                                       |             |             |              |              |
| Integumenta | ry system/appandage)       |                                       |             |             |              |              |
| lbcutis     | leukemic cell infiltration |                                       | <50><br>0   | <50><br>0   | <49><br>1    | <50><br>0    |
|             | metastasis:uterus tumor    |                                       | 0           | 1           | 0            | 0            |
| lespiratory | system}                    |                                       |             |             |              |              |
| Ung         | leukemic cell infiltration |                                       | <50><br>2   | <50><br>3   | <49><br>1    | <50><br>6    |
|             | metastasis:uterus tumor    |                                       | 0           | 0           | 1            | 2            |
|             | metastasis:adrenal tumor   |                                       | 0           | 1           | 0            | 0            |
|             | metastasis:pancreas tumor  |                                       | 1           | 0.          | 0            | 1            |
| lematopoiet | cic system)                |                                       |             |             |              |              |
| one marrow  | leukemic cell infiltration |                                       | <50><br>1   | <50><br>1   | <49><br>1    | <50><br>3    |
| mph node    | leukemic cell infiltration |                                       | <50><br>0   | <50><br>0   | <49><br>0    | <50><br>2    |
|             | metastasis:uterus tumor    |                                       | 0           | 0           | 1            | 1            |
| hymus       | metastasis:pancreas tumor  |                                       | <50><br>0   | <50><br>0   | <49><br>0    | <50><br>1    |
| oleen       | metastasis:uterus tumor    |                                       | <50><br>0   | <50><br>0   | <49><br>0    | <50><br>2    |
|             | metastasis:pancreas tumor  |                                       | 0           | 0           | 0            | 1            |

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

 $\overline{\phantom{a}}$ 

| SEX :         | FEMALE                     |                                       |             |             |              | PAGE :       |
|---------------|----------------------------|---------------------------------------|-------------|-------------|--------------|--------------|
| Drgan         | Findings                   | Group Name<br>No. of Animals on Study | 0 ppm<br>50 | 3 ppm<br>50 | 10 ppm<br>49 | 30 ppm<br>50 |
| {Circulatory  | system)                    |                                       |             |             |              |              |
| heart         | metastasis:pancreas tumor  |                                       | <50><br>1   | <50><br>0   | <49><br>0    | <50><br>0    |
| {Digestive sy | rstem)                     |                                       |             |             |              |              |
| stomach       | leukemic cell infiltration |                                       | <50><br>1   | <50><br>0   | <49><br>1    | <50><br>0    |
|               | metastasis:pancreas tumor  |                                       | 1           | 0           | 0            | 0            |
| small intes   | leukemic cell infiltration |                                       | <50><br>0   | <50><br>0   | <49><br>0    | <50><br>1    |
|               | metastasis:pancreas tumor  |                                       | 1           | 0           | 0            | 0            |
| large intes   | leukemic cell infiltration |                                       | <50><br>0   | <50><br>0   | <49><br>0    | <50><br>1    |
|               | metastasis:uterus tumor    |                                       | 0           | 0           | 0            | 1            |
|               | metastasis:pancreas tumor  |                                       | 1           | 0           | 0            | 0            |
| liver         | leukemic cell infiltration |                                       | <50><br>3   | <50><br>3   | <49><br>1    | <50><br>5    |
|               | metastasis:uterus tumor    |                                       | 0           | 0           | 0            | 3            |
|               | metastasis:pancreas tumor  |                                       | 1           | 0           | 0            | 1            |
| pancreas      | leukemic cell infiltration |                                       | <50><br>0   | <50><br>0   | <49><br>1    | <50><br>0    |
|               | metastasis:spleen tumor    |                                       | 0           | 0           | 1            | 0            |
| {Urinary syst | tem}                       |                                       |             |             |              |              |
| kidney        | leukemic cell infiltration |                                       | <50><br>0   | <50><br>0   | <49><br>0    | <50><br>1    |

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

b b : Number of animals with lesion

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

~

| SEX :         | FEMALE                     |                                       |             |             |                                       | PAGE :       |
|---------------|----------------------------|---------------------------------------|-------------|-------------|---------------------------------------|--------------|
| Organ         | Findings                   | Group Name<br>No. of Animals on Study | 0 ppm<br>50 | 3 ppm<br>50 | 10 ppm<br>49                          | 30 ppm<br>50 |
|               |                            | ······                                |             |             | · · · · · · · · · · · · · · · · · · · |              |
| {Urinary syst | tem)                       |                                       |             |             |                                       |              |
| kidney        | metastasis:uterus tumor    |                                       | <50><br>0   | <50><br>0   | < <b>49</b> ><br>1                    | <50><br>1    |
|               | metastasis:adrenal tumor   |                                       | 0           | 0           | 1                                     | 0            |
| urin bladd    | leukemic cell infiltration |                                       | <50><br>0   | <50><br>0   | <49><br>1                             | <50><br>0    |
| {Endocrine s  | ystem)                     |                                       |             |             |                                       |              |
| adrenal       | leukemic cell infiltration |                                       | <50><br>1   | <50><br>0   | <49><br>0                             | <50><br>2    |
|               | metastasis:uterus tumor    |                                       | 0           | 0           | 0                                     | 1            |
|               | metastasis:pancreas tumor  |                                       | 1           | 0           | 0                                     | 0            |
| {Reproductiv  | e system)                  |                                       |             |             |                                       |              |
| ovary         | leukemic cell infiltration |                                       | <50><br>0   | <50><br>1   | <49><br>0                             | <50><br>0    |
| uterus        | leukemic cell infiltration |                                       | <50><br>0   | <50><br>1   | <49><br>1                             | <50><br>0    |
| {Nervous sys  | tem)                       |                                       |             |             |                                       |              |
| brain         | leukemic cell infiltration |                                       | <50><br>1   | <50><br>0   | <49><br>1                             | <50><br>1    |
|               | metastasis:pituitary tumor |                                       | 2           | 4           | 0                                     | 1            |
| {Special sen  | nse organs/appendage)      |                                       |             |             |                                       |              |
| еўе           | leukemic cell infiltration |                                       | <50><br>0   | <50><br>0   | <49><br>0                             | <50><br>1    |

b b : Number of animals with lesion

| ANIMAL :<br>REPORT TYPE : | 0342<br>RAT F344/DuCrj<br>A1<br>FEMALE                                       |                                       | CAL FINDINGS : METAST/<br>LS (0-105W) | ASIS OF TUMOR (SUMMARY) |              | PAGE : 7     |
|---------------------------|------------------------------------------------------------------------------|---------------------------------------|---------------------------------------|-------------------------|--------------|--------------|
| Organ                     | Findings                                                                     | Group Name<br>No. of Animals on Study | 0 ppm<br>50                           | 3 ppm<br>50             | 10 ppm<br>49 | 30 ppm<br>50 |
| {Body cavities            | 5)                                                                           |                                       |                                       |                         |              |              |
| nediastinum               | metastasis:pancreas tumor                                                    |                                       | <50><br>1                             | <50><br>0               | <49><br>0    | <50><br>0    |
| peritoneum                | metastasis:spleen tumor                                                      |                                       | <50><br>0                             | <50><br>0               | <49><br>1    | <50><br>0    |
| (а)<br>b                  | a : Number of animals examined at the s<br>b : Number of animals with lesion | ite                                   |                                       |                         |              |              |
| (JPT150)                  |                                                                              |                                       |                                       |                         |              | BAI          |

APPENDIX N 5

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY RAT : FEMALE : DEAD AND MORIBUND ANIMALS (2-YEAR STUDY)

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

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|              |                            | Group Name              | 0 ppm     | 3 ppm     | 10 ppm    | 30 ppm    |
|--------------|----------------------------|-------------------------|-----------|-----------|-----------|-----------|
| Organ        | Findings                   | No. of Animals on Study | 9         | 12        | 10        | 18        |
| Tatogumoata  | ry system/appandage)       |                         |           |           |           |           |
|              | i y system appandage)      |                         |           |           |           |           |
| subcutis     | leukemic cell infiltration |                         | < 9><br>0 | <12><br>0 | <10><br>1 | <18><br>0 |
|              | metastasis:uterus tumor    |                         | 0         | 1         | 0         | 0         |
| Respiratory  | system)                    |                         |           |           |           |           |
| lung         | leukemic cell infiltration |                         | < 9><br>1 | <12><br>2 | <10><br>1 | <18><br>3 |
|              | metastasis:uterus tumor    |                         | 0         | 0         | 1         | 1         |
|              | metastasis:pancreas tumor  |                         | 1         | 0         | 0         | 1         |
| {Hematopoiet | ic system)                 |                         |           |           |           |           |
| one marrow   | leukemic cell infiltration |                         | < 9><br>1 | <12><br>1 | <10><br>1 | <18><br>3 |
| lymph node   | leukemic cell infiltration |                         | < 9><br>0 | <12><br>0 | <10><br>0 | <18><br>1 |
|              | metastasis:uterus tumor    |                         | 0         | 0         | 1         | 0         |
| thymus       | metastasis:pancreas tumor  |                         | < 9><br>0 | <12><br>0 | <10><br>0 | <18><br>1 |
| spleen       | metastasis:uterus tumor    |                         | < 9><br>0 | <12><br>0 | <10><br>0 | <18><br>2 |
|              | metastasis:pancreas tumor  |                         | 0         | 0         | 0         | 1         |
| {Circulatory | y system)                  |                         |           |           |           |           |
| heart        | metastasis:pancreas tumor  |                         | < 9><br>1 | <12><br>0 | <10><br>0 | <18><br>0 |

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

b b: Number of animals with lesion

(TPT150)

PAGE: 4

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

|               |                            | Group Name<br>No. of Animals on Study | 0 ppm<br>9 | 3 ppm<br>12 | 10 ppm<br>10 | 30 ppm<br>18 |
|---------------|----------------------------|---------------------------------------|------------|-------------|--------------|--------------|
| Organ         | Findings                   | ·····                                 |            |             |              |              |
| (D            |                            |                                       |            |             |              |              |
| {Digestive sy | stem)                      |                                       |            |             |              |              |
| stomach       | leukemic cell infiltration |                                       | < 9><br>1  | <12><br>0   | <10><br>1    | <18><br>0    |
|               | metastasis:pancreas tumor  |                                       | 1          | 0           | 0            | 0            |
| small intes   | metastasis:pancreas tumor  |                                       | < 9><br>1  | <12><br>0   | <10><br>0    | <18><br>0    |
| large intes   | metastasis:pancreas tumor  |                                       | < 9><br>1  | <12><br>0   | <10><br>0    | <18><br>0    |
| liver         | leukemic cell infiltration |                                       | < 9>       | <12><br>2   | <10><br>1    | <18><br>3    |
|               | metastasis:uterus tumor    |                                       | 0          | 0           | 0            | 2            |
|               | metastasis pancreas tumor  |                                       | 1          | 0           | 0            | 1            |
| pancreas      | leukemic cell infiltration |                                       | < 9><br>0  | <12><br>0   | <10><br>1    | <18><br>0    |
| {Urinary syst | em}                        |                                       |            |             |              |              |
| kidney        | leukemic cell infiltration |                                       | < 9><br>0  | <12><br>0   | <10><br>0    | <18><br>1    |
|               | metastasis:uterus tumor    |                                       | 0          | 0           | 1            | 0            |
|               | metastasis:adrenal tumor   |                                       | 0          | 0           | 1            | 0            |
| urin bladd    | leukemic cell infiltration |                                       | < 9><br>0  | <12><br>0   | <10><br>1    | <18><br>0    |
| {Endocrine sy | rstem)                     |                                       |            |             |              |              |
| adrenal       | leukemic cell infiltration |                                       | < 9><br>0  | <12><br>0   | <10><br>0    | <18><br>2    |

a : Number of animals examined at the sitebb : Number of animals with lesion

(IPT150)

PAGE : 5

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

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| 2X · PEMALE PAGE                     |                                                                        |                                           |            |             |                |              |
|--------------------------------------|------------------------------------------------------------------------|-------------------------------------------|------------|-------------|----------------|--------------|
| rgan                                 | Findings                                                               | Group Name<br>No. of Animals on Study<br> | 0 ppm<br>9 | 3 ppm<br>12 | - 10 ppm<br>10 | 30 ppm<br>18 |
| Endocrine sy                         | stem)                                                                  |                                           |            |             |                |              |
| irenal                               | S Lettij                                                               |                                           | < 9>       | <12>        | <10>           | <18>         |
| renal                                | metastasis:uterus tumor                                                |                                           | 0          | 0           | 0              | 1            |
|                                      | metastasis:pancreas tumor                                              |                                           | 1          | 0           | 0              | . 0          |
| eproductive                          | system}                                                                |                                           |            |             |                |              |
| ary                                  |                                                                        |                                           | < 9>       | <12>        | <10><br>0      | <18><br>0    |
|                                      | leukemic cell infiltration                                             |                                           | -          | 1           |                | -            |
| uterus<br>leukemic cell infiltration |                                                                        | < 9><br>0                                 | <12><br>1  | <10><br>1   | <18><br>0      |              |
| lervous syst                         | em)                                                                    |                                           |            |             |                |              |
| rain                                 |                                                                        |                                           | < 9>       | <12>        | <10>           | <18>         |
|                                      | leukemic cell infiltration                                             |                                           | 1          | 0           | 1              | 1            |
|                                      | metastasis:pituitary tumor                                             |                                           | 1          | 1           | 0              | 0            |
| pecial sens                          | e organs/appendage}                                                    |                                           |            |             |                |              |
| ye                                   | leukemic cell infiltration                                             |                                           | < 9>       | <12><br>0   | <10>           | <18>         |
|                                      | leukemic cell inilitration                                             |                                           | 0          | U           | 0              | 1            |
| Body cavitie                         | 25)                                                                    |                                           |            |             |                |              |
| ediastinum                           | metastasis:pancreas tumor                                              |                                           | < 9><br>1  | <12><br>0   | <10><br>0      | <18><br>0    |
| a><br>b                              | a : Number of animals examined at<br>b : Number of animals with lesion | the site                                  |            |             |                |              |

(JPT150)

PAGE: 6

APPENDIX N 6

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY RAT : FEMALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

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

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|                          |                            | Group Name              | 0 ppm     | 3 ppm<br>38 | 10 ppm<br>39 | 30 ppm<br>32 |
|--------------------------|----------------------------|-------------------------|-----------|-------------|--------------|--------------|
| Organ F                  | Findings                   | No. of Animals on Study | 41        | 38          | 39           | 32           |
| Respiratory              | system)                    |                         |           |             |              |              |
| Ung                      | leukemic cell infiltration |                         | <41><br>1 | <38><br>↓   | <39><br>0    | <32><br>3    |
|                          | metastasis:uterus tumor    |                         | 0         | ()          | 0            | 1            |
|                          | metastasis:adrenal tumor   |                         | 0         | 1           | 0            | 0            |
| Hematopoieti             | c system)                  |                         |           |             |              |              |
| ymph node                | leukemic cell infiltration |                         | <41><br>0 | <33><br>0   | <39><br>0    | <32><br>1    |
|                          | metastasis:uterus tumor    |                         | 0         | c           | 0            | 1            |
| Digestive sy             | stem}                      |                         |           |             |              |              |
| mall intes               | leukemic cell infiltration |                         | <41><br>0 | <38><br>0   | <39><br>0    | <32><br>1    |
| arge intes               | leukemic cell infiltration |                         | <41><br>0 | <38><br>0   | <39><br>0    | <32><br>1    |
|                          | metastasis:uterus tumor    |                         | 0         | 0           | 0            | 1            |
| iver                     | leukemic cell infiltration |                         | <41><br>2 | <38><br>1   | <39><br>0    | <32><br>2    |
|                          | metastasis:uterus tumor    |                         | 0         | 0           | 0            | 1            |
| ancreas                  | metastasis:spleen tumor    |                         | <41><br>0 | <:8><br>0   | <39><br>1    | <32><br>0    |
| Urinary sys <sup>.</sup> | tem)                       |                         |           |             |              |              |
| idney                    | metastasis:uterus tumor    |                         | <41><br>0 | <::8><br>0  | <39><br>0    | <32><br>1    |

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#### **`**,.... HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) SACRIFICED ANIMALS (105W)

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| PAGE : 3          |                                                                               |                                       |             |             |              |              |
|-------------------|-------------------------------------------------------------------------------|---------------------------------------|-------------|-------------|--------------|--------------|
| Organ             |                                                                               | Group Name<br>No. of Animals on Study | 0 ppm<br>41 | 3 ppm<br>38 | 10 ppm<br>39 | 30 ppm<br>32 |
| {Endocrine sy     | ystem}                                                                        |                                       |             |             |              |              |
| adrenal           | leukemic cell infiltration                                                    |                                       | <41><br>1   | <38><br>0   | <39><br>0    | <32><br>0    |
| {Nervous syst     | tem)                                                                          |                                       |             |             |              |              |
| brain             | metastasis:pituitary tumor                                                    |                                       | <41><br>1   | <38><br>3   | <39><br>0    | <32><br>1    |
| {Body cavition    | es)                                                                           |                                       |             |             |              |              |
| peritoneum        | metastasis:spleen tumor                                                       |                                       | <41><br>0   | <38><br>0   | <39><br>1    | <32><br>0    |
| <a>&gt;<br/>b</a> | a : Number of animals examined at the si<br>b : Number of animals with lesion | te                                    |             |             |              |              |
| (JPT150)          |                                                                               |                                       |             |             |              | BAIS         |

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APPENDIX O 1

IDENTITY AND IMPURITY OF GLYCIDOL IN THE 2-YEAR INHALATION STUDY

IDENTITY AND IMPURITY OF GLYCIDOL IN THE 2-YEAR INHALATION STUDY

Test Substance : Glycidol (Wako Pure Chemical Industries, Ltd.)

A. Lot No. : WTK5337

1. Spectral Data

Mass Spectrometry

Instrument

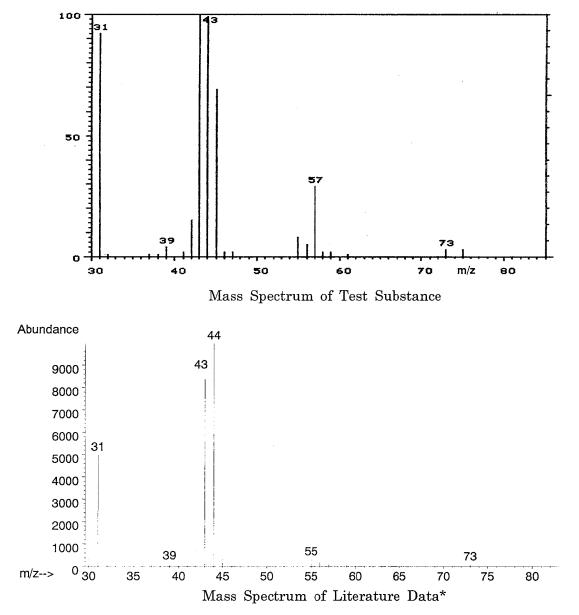
)

)

: Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Results: The mass spectrum was consistent with literature spectrum. (\*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 1733)

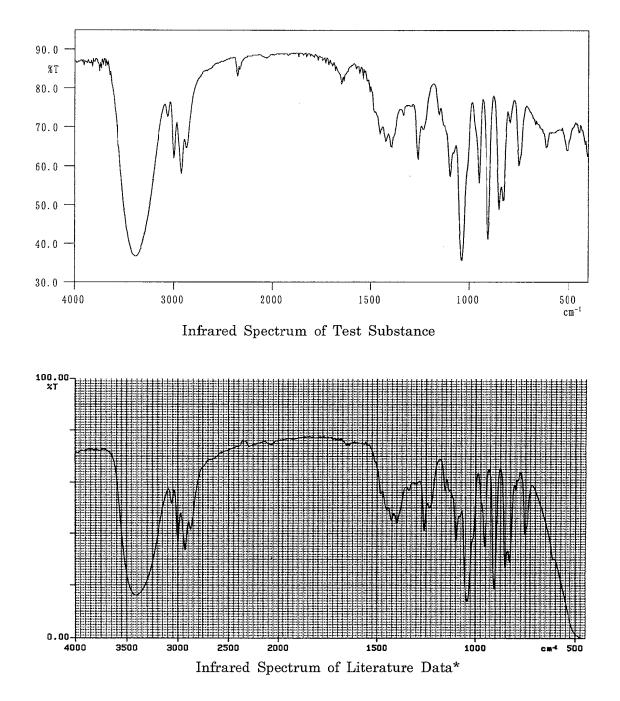
# Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

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

)



Results: The infrared spectrum was consistent with literature spectrum. (\*Performed by Wako Pure Chemical Industries, Ltd.)

### 2. Impurity

)

| Instrument        | : Hewlett Packard 5890A Gas Chromatograph       |  |  |  |  |
|-------------------|-------------------------------------------------|--|--|--|--|
| Column            | : Methyl Silicone (0.53 mm $\phi$ $	imes$ 60 m) |  |  |  |  |
| Column Temperatur | re: 150 °C                                      |  |  |  |  |
| Flow Rate         | : 10 mL/min                                     |  |  |  |  |
| Detector          | : FID (Flame Ionization Detector)               |  |  |  |  |
| Injection Volume  | :1 μL                                           |  |  |  |  |

| Sample Name    | Peak No. | Area<br>(%) | Peak Name                           |
|----------------|----------|-------------|-------------------------------------|
| Test Substance | 1        | 0.207       | Material which cannot be identified |
|                | 2        | 0.087       | Material which cannot be identified |
|                | 3        | 99.706      | glycidol                            |
|                |          |             |                                     |

- Results: Gas chromatography indicated one major peak (peak No.3) and two impurity peaks. These two impurity peaks(peaks No.1 and No.2) can not be identified. The amounts in the test substance were 0.207% and 0.087%.
- 3. Conclusion: The test substance was identified as glycidol by mass spectrum and infrared spectrum. Gas chromatography indicated one major peak(peak No.3) and two impurity peaks. These two impurity peaks(peaks No.1 and No.2) can not be identified. The amounts in the test substance were 0.207% and 0.087%.

B. Lot No. : PAL5331

1. Spectral Data

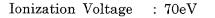
)

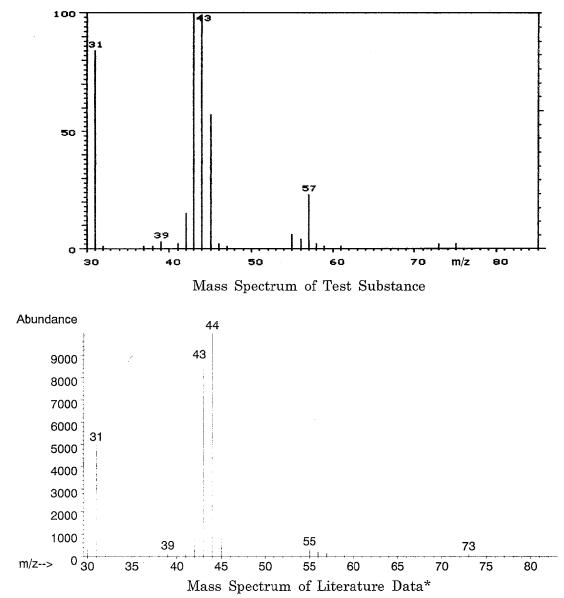
)

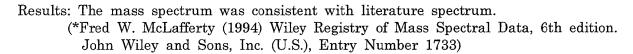
Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)







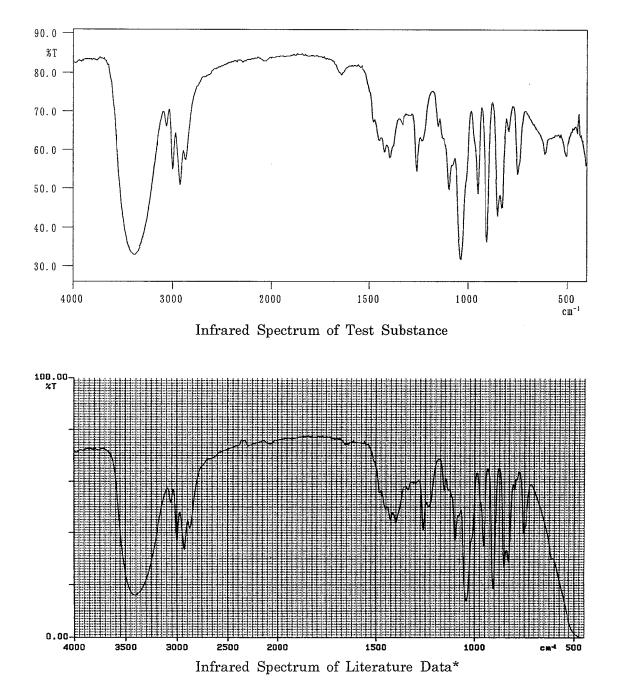
# Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm<sup>-1</sup>

)



Results: The infrared spectrum was consistent with literature spectrum. (\*Performed by Wako Pure Chemical Industries, Ltd.)

# 2. Impurity

)

| Instrument        | : Hewlett Packard 5890A Gas Chromatograph       |
|-------------------|-------------------------------------------------|
| Column            | : Methyl Silicone (0.53 mm $\phi$ $	imes$ 60 m) |
| Column Temperatur | re: 150 °C                                      |
| Flow Rate         | : 10 mL/min                                     |
| Detector          | : FID (Flame Ionization Detector)               |
| Injection Volume  | : 1 μL                                          |
|                   |                                                 |

| Sample Name    | Peak No. | Area<br>(%)    | Peak Name                           |
|----------------|----------|----------------|-------------------------------------|
| Test Substance | 1        | 0.215          | Material which cannot be identified |
|                | 2        | 0.083          | Material which cannot be identified |
|                | 3        | <b>99.7</b> 02 | glycidol                            |
|                |          |                |                                     |

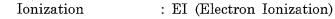
- Results: Gas chromatography indicated one major peak (peak No.3) and two impurity peaks. These two impurity peaks(peaks No.1 and No.2) can not be identified. The amounts in the test substance were 0.215% and 0.083%.
- 3. Conclusion: The test substance was identified as glycidol by mass spectrum and infrared spectrum. Gas chromatography indicated one major peak(peak No.3) and two impurity peaks. These two impurity peaks(peaks No.1 and No.2) can not be identified. The amounts in the test substance were 0.215% and 0.083%.

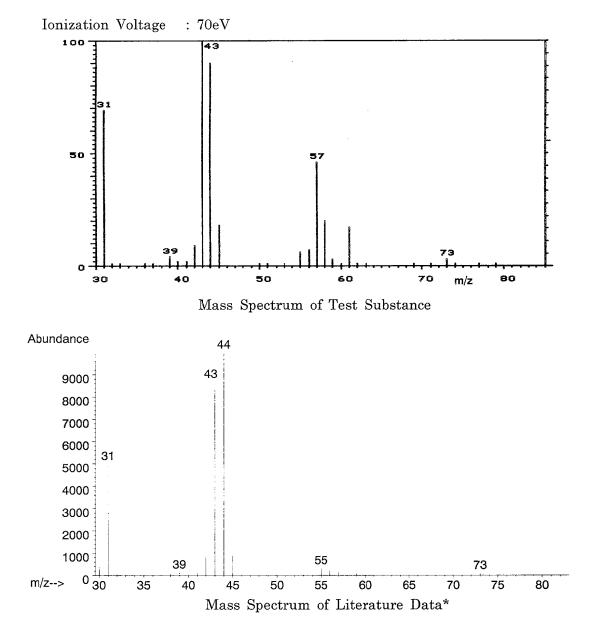
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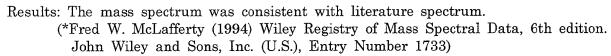
)

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer







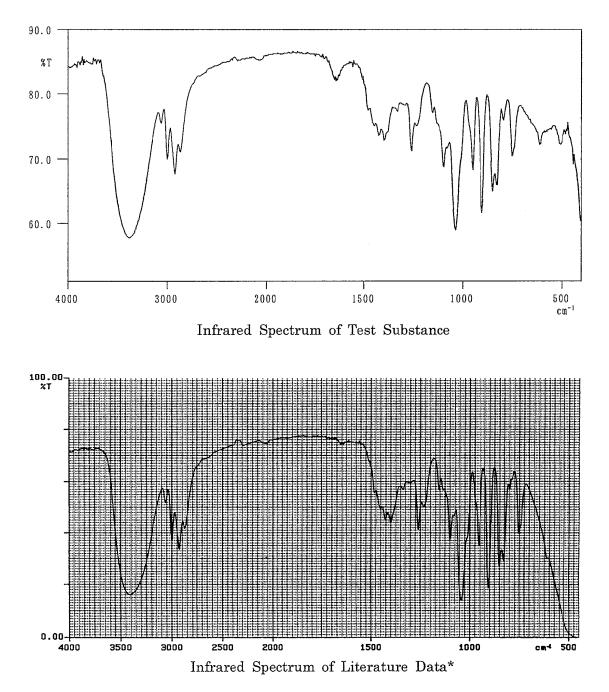
# Infrared Spectrometry



Cell : KBr Liquid Cell

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

)



Results: The infrared spectrum was consistent with literature spectrum. (\*Performed by Wako Pure Chemical Industries, Ltd.)

# 2. Impurity

)

| Instrument        | : Hewlett Packard 5890A Gas Chromatograph       |
|-------------------|-------------------------------------------------|
| Column            | : Methyl Silicone (0.53 mm $\phi$ $	imes$ 60 m) |
| Column Temperatur | re: 150 °C                                      |
| Flow Rate         | : 10 mL/min                                     |
| Detector          | : FID (Flame Ionization Detector)               |
| Injection Volume  | :1 μL                                           |
|                   |                                                 |
|                   | Deale Maria                                     |

| Sample Name    | Peak No. | Area<br>(%)    | Peak Name                           |
|----------------|----------|----------------|-------------------------------------|
| Test Substance | 1        | 0.220          | Material which cannot be identified |
|                | 2        | 0.087          | Material which cannot be identified |
|                | 3        | <b>99.69</b> 3 | glycidol                            |
|                |          |                |                                     |

- Results: Gas chromatography indicated one major peak (peak No.3) and two impurity peaks. These two impurity peaks(peaks No.1 and No.2) can not be identified. The amounts in the test substance were 0.220% and 0.087%.
- 3. Conclusion: The test substance was identified as glycidol by mass spectrum and infrared spectrum. Gas chromatography indicated one major peak(peak No.3) and two impurity peaks. These two impurity peaks(peaks No.1 and No.2) can not be identified. The amounts in the test substance were 0.220% and 0.087%.

APPENDIX O 2

STABILITY OF GLYCIDOL IN THE 2-YEAR INHALATION STUDY

# STABILITY OF GLYCIDOL IN THE 2-YEAR INHALATION STUDY

| Test Substance        | : Glycidol (Wako Pure Chemical Industries, Ltd.)                                                       |
|-----------------------|--------------------------------------------------------------------------------------------------------|
| A. Lot No.            | : WTK5337                                                                                              |
| 1. Sample             | : This lot was used from 1997.9.29 to 1998.8.5. Test substance was stored at a temperature below 20°C. |
| 2. Gas Chromatography | <b>7</b>                                                                                               |
| Instrument            | : Hewlett Packard 5890A Gas Chromatograph                                                              |
| Column                | : Methyl Silicone ( 0.53 mm $\phi$ $	imes$ 60 m)                                                       |
| Column Temperatur     | re: 150° C                                                                                             |
| Flow Rate             | : 10 mL/min                                                                                            |
| Detector              | : FID (Flame Ionization Detector)                                                                      |
| Injection Volume      | : 1 μL                                                                                                 |

| Date<br>(date analyzed) | Peak No. | Retention Time<br>(min) | Area<br>(%) |
|-------------------------|----------|-------------------------|-------------|
| 1997.09.26              | 1        | 1.914                   | 0.207       |
|                         | 2        | 2.217                   | 0.087       |
|                         | 3        | 2.560                   | 99.706      |
| 1998.08.06              | 1        | 1.901                   | 0.217       |
|                         | 2        | 2.205                   | 0.088       |
|                         | 3        | 2.549                   | 99.695      |

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- Results: Gas chromatography indicated one major peak (peak No.3) and two impurities (peaks No.1 and No.2 < 0.4% of total area) analyzed on 1997.9.26 and one major peak (peak No.3) and two impurities (peaks No.1 and No.2 < 0.4% of total area) analyzed on 1998.8.6. No new trace impurity peak in the test substance analyzed on 1998.8.6 was detected.
- 3. Conclusions: The test substance was stable for about 1 year at a temperature below  $20^{\circ}$ C.

| B. Lot No.          | : PAL5331                                                                                             |
|---------------------|-------------------------------------------------------------------------------------------------------|
| 1. Sample           | : This lot was used from 1998.8.6 to 1999.4.6. Test substance was stored at a temperature below 20°C. |
| 2. Gas Chromatogray | phy                                                                                                   |
| Instrument          | : Hewlett Packard 5890A Gas Chromatograph                                                             |
| Column              | : Methyl Silicone ( 0.53 mm $\phi$ $	imes$ 60 m)                                                      |
| Column Tempera      | ture: 150°C                                                                                           |
| Flow Rate           | : 10 mL/min                                                                                           |
| Detector            | : FID (Flame Ionization Detector)                                                                     |
|                     |                                                                                                       |

Injection Volume : 1 µL

| Date<br>(date analyzed) | Peak No. | Retention Time<br>(min) | Area<br>(%)    |
|-------------------------|----------|-------------------------|----------------|
| 1998.07.27              | 1        | 1.908                   | 0.215          |
|                         | 2        | 2.210                   | 0.083          |
|                         | 3        | 2.554                   | <b>99</b> .702 |
| 1999.04.07              | 1        | 1.902                   | 0.218          |
|                         | 2        | 2.203                   | 0.086          |
|                         | 3        | 2.545                   | 99.696         |

- Results: Gas chromatography indicated one major peak (peak No.3) and two impurities (peaks No.1 and No.2 < 0.4% of total area) analyzed on 1998.7.27 and one major peak (peak No.3) and two impurities (peaks No.1 and No.2 < 0.4% of total area) analyzed on 1999.4.7. No new trace impurity peak in the test substance analyzed on 1999.4.7 was detected.
- 3. Conclusions: The test substance was stable for about 8 months at a temperature below  $20^{\circ}$ C.

- 1. Sample : This lot was used from 1999.4.7 to 1999.9.24. Test substance was stored at a temperature below 20°C.
- 2. Gas Chromatography

| Instrument        | : Hewlett Packard 5890A Gas Chromatograph        | 1 |
|-------------------|--------------------------------------------------|---|
| Column            | : Methyl Silicone ( 0.53 mm $\phi$ $	imes$ 60 m) |   |
| Column Temperatur | : 150° C                                         |   |
| Flow Rate         | : 10 mL/min                                      |   |
| Detector          | : FID (Flame Ionization Detector)                |   |
| Injection Volume  | :1 μL                                            |   |

: CKP4929

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| Date<br>(date analyzed) | Peak No. | Retention Time<br>(min) | Area<br>(%) |
|-------------------------|----------|-------------------------|-------------|
| 1999.04.06              | 1        | 1.900                   | 0.220       |
|                         | 2        | 2.205                   | 0.087       |
|                         | 3        | 2.547                   | 99.693      |
| 1999.10.28              | 1        | 1.897                   | 0.220       |
|                         | 2        | 2.203                   | 0.081       |
|                         | 3        | 2.544                   | 99.699      |

- Results: Gas chromatography indicated one major peak (peak No.3) and two impurities (peaks No.1 and No.2 < 0.4% of total area) analyzed on 1999.4.6 and one major peak (peak No.3) and two impurities (peaks No.1 and No.2 < 0.4% of total area) analyzed on 1999.10.28. No new trace impurity peak in the test substance analyzed on 1999.10.28 was detected.
- 3. Conclusions: The test substance was stable for about 7 months at a temperature below  $20^{\circ}$ C.

APPENDIX P 1

CONCENTRATION OF GLYCIDL IN THE INHALATION CHAMBER OF THE 2-YEAR INHALATION STUDY

# CONCENTRATION OF GLYCIDOL IN THE INHALATION CHAMBER OF THE 2-YEAR INHALATION STUDY

| Concentration (ppm) |
|---------------------|
| Mean ± S.D.         |
| $0.0 \pm 0.0$       |
| $3.0 \pm 0.1$       |
| $10.0 \pm 0.2$      |
| $29.9 \pm 0.6$      |
|                     |

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APPENDIX P 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-YEAR INHALATION STUDY OF GLYCIDOL

# ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-YEAR INHALATION STUDY OF GLYCIDOL

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| Group | Temperature(°C) | Humidity(%)    | Ventilation Rate<br>(L/min) | Air Changes<br>(time/h) |
|-------|-----------------|----------------|-----------------------------|-------------------------|
| Name  | Mean $\pm$ S.D. | Mean ± S.D.    | Mean $\pm$ S.D.             | Mean                    |
| 0ppm  | $22.2 \pm 0.2$  | $54.8 \pm 1.1$ | $1521.2 \pm 10.6$           | 12.0                    |
| 3ppm  | $22.5 \pm 0.3$  | $54.1 \pm 1.2$ | $1516.9 \pm 14.3$           | 12.0                    |
| 10ppm | $22.1 \pm 0.2$  | 54.5 $\pm$ 1.8 | $1521.5 \pm 10.3$           | 12.0                    |
| 30ppm | $22.1 \pm 0.2$  | $53.3 \pm 2.4$ | $1515.5 \pm 10.5$           | 12.0                    |

APPENDIX Q

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-YEAR INHALATION STUDY OF GLYCIDOL

# METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-YEAR INHALATION STUDY OF GLYCIDOL

| Item                                                | Method                                         | Unit                  | Decimal<br>place |
|-----------------------------------------------------|------------------------------------------------|-----------------------|------------------|
| Hematology                                          |                                                |                       |                  |
| Red blood cell (RBC)                                | Light scattering method <sup>1)</sup>          | ×10 <sup>6</sup> /µL  | 2                |
| Hemoglobin(Hgb)                                     | Cyanmethemoglobin method <sup>1)</sup>         | g/dL                  | 1                |
| Hematocrit(Hct)                                     | Calculated as RBC×MCV/10 $^{10}$               | %                     | 1                |
| Mean corpuscular volume(MCV)                        | Light scattering method <sup>1)</sup>          | fL                    | 1                |
| Mean corpuscular hemoglobin(MCH)                    | Calculated as Hgb/RBC $\times 10^{10}$         | Pg                    | 1                |
| Mean corpuscular hemoglobin concentration<br>(MCHC) | Calculated as Hgb/Hct $\times 100^{10}$        | g/dL                  | 1                |
| Platelet                                            | Light scattering method <sup>1)</sup>          | $\times 10^{3}/\mu L$ | 0                |
| White blood cell(WBC)                               | Light scattering method <sup>1)</sup>          | ×10³/µL               | 2                |
| Differential WBC                                    | Pattern recognition method <sup>29</sup>       | %                     | 0                |
|                                                     | (Wright staining)                              |                       |                  |
| Biochemistry                                        |                                                |                       |                  |
| Total protein(TP)                                   | Biuret method <sup>3)</sup>                    | g/dL                  | 1                |
| Albumin (Alb)                                       | BCG method <sup>3)</sup>                       | g/dL                  | 1                |
| A/G ratio                                           | Calculated as $Alb/(TP - Alb)^{3)}$            | -                     | 1                |
| T-bilirubin                                         | Alkaline azobilirubin method <sup>3)</sup>     | mg/dL                 | 2                |
| Glucose                                             | GlcK·G-6-PDH method <sup>3)</sup>              | mg/dL                 | 0                |
| T-cholesterol                                       | CE•COD•POD method <sup>3)</sup>                | mg/dL                 | 0                |
| Triglyceride                                        | LPL•GK•GPO•POD method <sup>3)</sup>            | mg/dL                 | 0                |
| Phospholipid                                        | PLD·ChOD·POD method <sup>3)</sup>              | mg/dL                 | 0                |
| Glutamic oxaloacetic transaminase (GOT)             | JSCC method <sup>3)</sup>                      | IU/L                  | 0                |
| Glutamic pyruvic transaminase (GPT)                 | JSCC method <sup>8</sup>                       | IU/L                  | 0                |
| Lactate dehydrogenase (LDH)                         | SFBC method <sup>3)</sup>                      | IU/L                  | 0                |
| Alkaline phosphatase (ALP)                          | GSCC method <sup>3)</sup>                      | IU/L                  | 0                |
| $\gamma$ -Glutamyl transpeptidase ( $\gamma$ -GTP)  | L- $\gamma$ -Glutamyl-p-nitroanilide method 3) | IU/L                  | 0                |
| Creatine phosphokinase (CPK)                        | JSCC method <sup>3)</sup>                      | IU/L                  | 0                |
| Urea nitrogen                                       | Urease • GLDH method $^{3)}$                   | mg/dL                 | 1                |
| Creatinine                                          | Jaffe method $^{3)}$                           | mg/dL                 | 1                |
| Sodium                                              | Ion selective electrode method <sup>3)</sup>   | mEq/L                 | 0                |
| Potassium                                           | Ion selective electrode method $^{3)}$         | mEq/L                 | 1                |
| Chloride                                            | Ion selective electrode method $^{\circ)}$     | mEq/L                 | 0                |
| Calcium                                             | OCPC method <sup>3)</sup>                      | mg/dL                 | 1                |
| Inorganic phosphorus                                | PNP·XOD·POD method <sup>3)</sup>               | mg/dL                 | 1                |

1) Automatic blood cell analyzer (Technicon H·1 : Bayer Corporation)

2) Automatic blood cell differential analyzer (MICROX HEG-120NA : OMRON Corporation )

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

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