P - クロロニトロベンゼンのラット及びマウスを用いた
経口（混餌）によるがん原性試験結果報告書

APPENDIX

(C1-1～C12-4)

13ｗｅｅｋ　STUDY　NO.　0057 ; 0058

中央労働災害防止協会
日本バイオアッセイ研究センター

APPENDIX C 1-1

CLINICAL OBSERVATION (THIRTEEN-WEEK STUDIES: SUMMARY)

RAT: MALE

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 0-0 1	1-7 1	2-7 1	3-7 1	4-7 1	5-7 1	6-7 1	7-7 1	8-7 1	9-7 1	10-7 1	11-7 1	12-7 1	13-7 1
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	1	1	1	1	1	1	0	0	0	0	0	0
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	1	1	1	1	1	1	0	0	0	0	0	0	0
WASTING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	1	1	0	0	1	1	0	0	0	0	0	0	0
COLORED	Control	0	0	0	0	0	0	1	0	0	0	0	0	0	0
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	1	1	0	0	0	0	0
	667 ppm	0	0	0	0	1	1	0	2	0	1	0	0	0	2
	2000 ppm	0	0	3	1	7	8	4	6	4	2	1	3	3	9
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	1	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	1	4	1	1	2	1	1	0	0	0	0	0	0

Clinical sign	Group Name	Administration Week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
TRAUMA	Control	0	0	0	0	0	0	0	0	1	0	0	0	0	0
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SOILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	2
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	2	0	1	0	0	0	1
	667 ppm	0	0	0	1	0	0	0	3	0	0	0	0	0	1
	2000 ppm	0	1	2	1	0	1	0	2	1	0	0	0	0	4
GUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EYE HEMORRHAGIC DISCHA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	1
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	1	0	1	1	1	1	1
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	1	0	0	0	0	0	0	0	0
SORE OF SOLE	Control	0	0	0	0	0	0	0	0	0	0	0	0	1	2
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	1	3	4	8
	74.1 ppm	0	0	0	0	0	0	0	1	1	1	1	1	3	5
	222 ppm	0	0	0	0	0	0	0	0	0	0	1	5	8	9
	667 ppm	0	0	0	0	0	0	0	0	0	1	4	6	7	9
	2000 ppm	0	0	0	0	0	0	0	1	1	3	8	9	10	10

Clinical sign	Group Name	Administration Week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
NOSE HEMORRHAGIC DISCHA	Control	0	0	1	1	3	3	2	1	0	1	2	1	1	0
	24.7 ppm	0	0	2	0	5	2	0	2	0	0	1	1	3	0
	74.1 ppm	0	0	1	0	2	0	0	3	1	0	0	0	1	0
	222 ppm	0	0	2	0	4	2	1	4	1	0	1	0	1	3
	667 ppm	0	0	2	0	0	1	0	0	0	0	1	0	1	1
	2000 ppm	0	1	0	0	0	0	0	0	0	0	0	0	0	0
NOSE SEROUS DISCHARGE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	1	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ANEMIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	1	1	1	2	2	1	5	5	5
	667 ppm	0	10	10	10	10	10	10	10	10	10	10	10	10	10
	2000 ppm	0	10	10	10	10	10	10	10	10	10	10	10	10	10
LOOSE STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	24.7 ppm	0	0	0	0	0	0	0	0	1	0	0	0	1	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	1	0	1	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	1	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SALIVATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	1	0	0	0	0	0	0	0	0	0	0	0	0

APPENDIX C 1-2

CLINICAL OBSERVATION (THIRTEEN-WEEK STUDIES: SUMMARY)

RAT: FEMALE

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 0-0 1	1-7 1	2-7 1	3-7 1	4-7 1	5-7 1	6-7 1	7-7 1	8-7 1	9-7 1	10-7 1	11-7 1	12-7 1	13-7 1
COLORED	Control	0	0	0	0	0	0	0	0	1	0	2	1	2	2
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	0
	74.1 ppm	0	0	0	0	0	0	1	1	1	1	2	1	2	3
	222 ppm	0	0	0	0	1	1	1	1	2	2	2	1	2	3
	667 ppm	0	0	6	2	3	3	3	3	5	4	4	4	4	10
	2000 ppm	0	0	9	6	6	6	4	5	5	4	7	4	7	10
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	3	1	1	1	0	0	0	0	0	0	0	0
LOSS OF HAIR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	1	1	1	1
SOILED PERI GENITALIA	Control	0	0	0	0	0	0	1	0	1	0	0	0	0	5
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	74.1 ppm	0	0	0	0	1	1	0	0	1	0	1	1	0	3
	222 ppm	0	0	0	0	1	0	0	0	1	1	0	0	0	2
	667 ppm	0	0	5	1	2	0	0	0	1	0	0	2	1	7
	2000 ppm	0	1	6	2	4	1	1	0	2	1	4	6	1	7
LACRYMATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	1	1	0	1
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 0-0 1	1-7 1	2-7 1	3-7 1	4-7 1	5-7 1	6-7 1	7-7 1	8-7 1	9-7 1	10-7 1	11-7 1	12-7 1	13-7 1
GUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	1	2
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	0	1	4	3
	74.1 ppm	0	0	0	0	0	1	0	0	0	0	0	1	1	3
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	1	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
EYE HEMORRHAGIC DISCHA	Control	0	0	0	0	0	0	0	0	0	0	0	1	1	0
	24.7 ppm	0	0	0	0	0	0	0	1	0	0	0	0	0	1
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	1	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	1	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SORE OF SOLE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	1	1	1
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	1
NOSE HEMORRHAGIC DISCHA	Control	0	0	1	0	0	2	0	1	0	0	0	0	0	1
	24.7 ppm	0	0	0	0	1	0	2	3	0	0	0	0	1	1
	74.1 ppm	0	0	3	0	2	1	0	2	0	0	0	0	1	0
	222 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	2	1	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ANEMIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	24.7 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	2	9	9	9	10	10	10	10	10
	667 ppm	0	10	10	10	10	10	10	10	10	10	10	10	10	10
	2000 ppm	0	10	10	10	10	10	10	10	10	10	10	10	10	10

Clinical sign	Group Name	Administration Week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
SALIVATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	24.7 ppm	0	0	0	0	0	0	0	0	0	1	0	0	0	0
	74.1 ppm	0	0	0	0	0	1	0	0	0	0	0	0	0	0
	222 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

APPENDIX C 1-3

CLINICAL OBSERVATION (THIRTEEN-WEEK STUDIES: SUMMARY)

MOUSE: MALE

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 0-0 1	1-7 1	2-7 1	3-7 1	4-7 1	5-7 1	6-7 1	7-7 1	8-7 1	9-7 1	10-7 1	11-7 1	12-7 1	13-7 1
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000 ppm	0	0	0	0	0	0	0	0	0	0	1	0	0	0
TREMOR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	1	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
WASTING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	0
COLORED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	1	4	4	0	2	1
	6000 ppm	0	0	1	0	0	0	1	1	1	5	5	4	4	2
LOSS OF HAIR	Control	0	0	4	6	6	7	7	7	7	7	7	7	7	7
	74.1 ppm	0	0	1	3	4	4	5	4	6	6	6	6	6	6
	222 ppm	0	1	4	6	6	6	5	5	6	6	7	7	7	6
	667 ppm	0	1	2	3	3	4	3	3	5	4	4	4	4	4
	2000 ppm	0	1	2	4	5	6	4	5	5	6	6	7	7	5
	6000 ppm	0	1	2	3	4	4	1	1	1	1	2	3	3	4

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
SOILED PERI GENITALIA	Control	0	0	0	0	0	0	0	1	1	1	0	0	0	0
	74.1 ppm	0	0	0	0	1	0	1	0	1	0	2	1	2	1
	222 ppm	0	0	0	1	4	3	2	1	2	3	6	3	3	2
	667 ppm	0	0	0	0	1	0	0	1	2	0	0	1	1	0
	2000 ppm	0	0	0	2	2	2	3	1	2	3	3	3	4	0
	6000 ppm	0	0	1	0	1	0	0	1	1	2	2	2	3	1
ANEMIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	3	3	7	9	9	10	10	10	10	10	10
	6000 ppm	0	10	10	10	10	10	10	10	10	10	10	10	10	10

APPENDIX C 1-4

CLINICAL OBSERVATION (THIRTEEN-WEEK STUDIES: SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000 ppm	0	0	0	0	0	0	0	1	1	1	1	1	1	1
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000 ppm	0	0	1	1	0	0	0	0	0	0	0	0	0	0
LATERAL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000 ppm	0	0	0	0	0	0	0	1	0	0	0	0	0	0
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	1	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000 ppm	0	3	3	1	0	0	0	0	0	0	0	0	0	0
WASTING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	1	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 0-0 1	1-7 1	2-7 1	3-7 1	4-7 1	5-7 1	6-7 1	7-7 1	8-7 1	9-7 1	10-7 1	11-7 1	12-7 1	13-7 1
SOILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	1	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000 ppm	0	1	0	0	0	0	0	0	0	0	0	0	0	0
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	1	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000 ppm	0	0	6	1	0	0	0	0	0	0	0	0	0	0
LOSS OF HAIR	Control	0	0	1	1	2	3	4	4	4	6	6	6	7	7
	74.1 ppm	0	3	4	3	4	4	5	6	6	6	6	6	6	6
	222 ppm	0	2	2	3	5	7	9	9	9	9	9	9	10	10
	667 ppm	0	1	3	5	5	7	7	8	8	9	9	9	9	8
	2000 ppm	0	0	1	3	5	5	3	3	4	5	6	5	5	3
	6000 ppm	0	0	0	0	1	2	1	1	2	2	2	4	4	3
TRAUMA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	1	0	0	0	0	0	0	0
	6000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ANEMIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	10	10	9	9	10	10	10	10	10	10	10	10	10
	6000 ppm	0	10	10	10	10	10	10	10	9	9	9	9	9	9

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
SALIVATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	74.1 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	667 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000 ppm	0	0	0	0	0	0	0	1	0	0	0	0	0	0

APPENDIX C 2-1

BODY WEIGHT CHANGES (THIRTEEN-WEEK STUDIES : SUMMARY)

RAT : MALE

STUDY NO. : 0057
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	129± 4	163± 8	196± 10	224± 8	244± 10	262± 10	272± 11
24.7 ppm	129± 4	164± 6	198± 8	226± 7	246± 6	266± 6	280± 7
74.1 ppm	129± 4	166± 6	202± 7	228± 9	248± 6	266± 6	279± 6
222 ppm	129± 4	164± 6	199± 7	227± 5	248± 5	268± 5	283± 6
667 ppm	129± 4	159± 6	194± 7	221± 7	242± 8	262± 11	277± 11
2000 ppm	129± 4	132± 19**	161± 22**	187± 22**	211± 20**	226± 40*	242± 30

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

STUDY NO. : 0057
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	285± 11	293± 12	303± 13	309± 15	315± 15	321± 15	326± 16
24.7 ppm	293± 10	304± 11	314± 12	324± 13	334± 13*	341± 14**	347± 13**
74.1 ppm	293± 7	301± 7	310± 7	318± 7	326± 6	332± 7	339± 6
222 ppm	289± 25	305± 9	316± 9	326± 11*	334± 12*	341± 12**	349± 12**
667 ppm	290± 12	303± 13	313± 13	323± 13	330± 15	338± 15*	344± 16*
2000 ppm	259± 22	273± 20	286± 17*	297± 16	306± 15	314± 16	317± 15

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX C 2-2

BODY WEIGHT CHANGES (THIRTEEN-WEEK STUDIES : SUMMARY)

RAT : FEMALE

STUDY NO. : 0057
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	100± 4	117± 5	131± 6	142± 8	149± 8	158± 10	164± 12
24.7 ppm	100± 5	118± 5	132± 6	144± 6	152± 6	162± 7	168± 7
74.1 ppm	100± 5	117± 5	131± 5	142± 6	150± 5	161± 7	168± 7
222 ppm	100± 4	115± 4	128± 4	140± 5	147± 7	158± 6	165± 8
667 ppm	100± 5	113± 4	126± 3	139± 5	148± 5	156± 7	165± 7
2000 ppm	100± 5	100± 5**	114± 7**	126± 10**	136± 8**	145± 7**	151± 7**

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

STUDY NO. : 0057
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	169± 14	173± 15	173± 15	178± 16	181± 17	185± 17	187± 17
24.7 ppm	174± 8	178± 9	183± 10	187± 9	190± 10	193± 10	192± 11
74.1 ppm	173± 8	179± 8	183± 7	186± 8	189± 8	192± 8	193± 8
222 ppm	170± 11	177± 12	179± 13	184± 12	187± 12	190± 11	192± 12
667 ppm	169± 9	175± 8	180± 10	184± 9	186± 7	190± 9	191± 7
2000 ppm	157± 6*	163± 7	165± 7	171± 7	173± 7	176± 8	179± 9

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

APPENDIX C 2-3

BODY WEIGHT CHANGES (THIRTEEN-WEEK STUDIES: SUMMARY)

MOUSE: MALE

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	22.7± 0.8	22.8± 1.7	25.5± 1.2	26.1± 1.3	27.1± 1.6	27.9± 1.4	28.4± 1.5
74.1 ppm	22.6± 0.9	23.3± 1.4	25.8± 1.0	26.6± 0.9	27.3± 1.0	27.7± 1.0	28.5± 1.3
222 ppm	22.7± 0.8	23.4± 1.6	25.2± 1.0	25.9± 1.0	26.9± 1.4	27.7± 1.4	28.9± 1.6
667 ppm	22.7± 0.8	22.7± 1.2	25.2± 1.2	25.6± 1.6	27.3± 1.8	27.4± 1.6	28.2± 1.5
2000 ppm	22.7± 0.9	23.2± 0.9	24.4± 0.7	25.1± 1.1	26.4± 1.1	26.3± 1.0	27.5± 1.1
6000 ppm	22.7± 0.9	20.2± 1.1**	20.4± 1.2**	21.0± 1.5**	22.6± 1.8**	22.9± 2.3**	24.2± 2.1**

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	29.2± 1.3	30.0± 2.0	30.3± 2.2	31.1± 2.2	30.7± 2.0	32.2± 2.4	33.1± 2.2
74.1 ppm	28.9± 1.3	30.6± 1.3	30.7± 1.4	32.4± 1.3	32.2± 2.5	33.7± 1.9	33.9± 1.8
222 ppm	29.6± 1.9	30.7± 2.0	31.0± 1.8	32.5± 2.2	32.0± 2.1	33.7± 2.2	34.9± 2.4
667 ppm	29.5± 2.1	30.5± 2.1	30.9± 2.3	32.2± 2.5	31.9± 2.8	33.6± 2.8	35.4± 2.9
2000 ppm	28.0± 1.2	28.8± 1.4	29.0± 1.5	30.2± 1.4	29.6± 1.9	31.4± 1.6	32.5± 2.0
6000 ppm	25.1± 1.7**	26.4± 2.0**	26.7± 2.4**	27.1± 2.1**	27.6± 1.8*	27.7± 1.8**	28.2± 1.9**

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX C 2-4

BODY WEIGHT CHANGES (THIRTEEN-WEEK STUDIES: SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	19.1± 0.6	19.2± 0.6	19.8± 0.4	20.1± 0.6	20.1± 1.5	20.9± 0.6	22.0± 1.0
74.1 ppm	19.1± 0.6	19.4± 0.8	20.1± 0.7	20.2± 0.8	20.2± 1.0	21.3± 1.1	22.1± 1.0
222 ppm	19.1± 0.6	19.8± 0.7	20.2± 0.9	20.7± 1.2	20.2± 1.2	21.4± 0.7	22.9± 1.2
667 ppm	19.1± 0.6	19.7± 0.5	20.2± 0.4	20.1± 0.7	21.1± 1.3	21.6± 1.0	22.6± 0.7
2000 ppm	19.1± 0.6	19.6± 0.5	20.3± 0.8	20.6± 0.6	20.9± 1.1	22.5± 0.6**	22.8± 0.9
6000 ppm	19.1± 0.6	15.8± 0.7**	17.0± 0.8**	17.9± 0.9**	19.1± 1.1	19.6± 1.1**	20.3± 1.2**

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

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	21.9± 1.0	22.4± 1.0	22.8± 1.0	23.7± 1.2	22.0± 1.1	24.2± 1.0	24.3± 1.6
74.1 ppm	22.5± 1.0	23.3± 1.2	23.7± 1.0	24.4± 1.5	23.4± 0.8	25.6± 0.9	25.7± 1.5
222 ppm	23.0± 1.6	23.6± 1.4*	23.0± 3.8	25.2± 1.8	24.6± 2.0**	26.0± 1.7	26.4± 2.6
667 ppm	23.1± 1.0	23.4± 0.9	23.8± 1.0	24.7± 1.2	24.0± 1.5**	25.9± 1.7	26.0± 1.7
2000 ppm	23.3± 1.2*	23.6± 0.9	24.2± 1.2	25.2± 1.0	24.4± 1.3**	25.5± 0.9	25.7± 1.3
6000 ppm	20.7± 0.9	21.0± 1.0*	21.5± 1.0	21.9± 1.0*	22.6± 0.9	22.9± 0.7	23.0± 0.6

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX C 3-1

FOOD CONSUMPTION CHANGES (THIRTEEN-WEEK STUDIES: SUMMARY)

RAT: MALE

STUDY NO. : 0057
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1. 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	13.6± 0.9	14.4± 0.9	15.4± 0.9	15.0± 0.8	15.1± 0.8	14.8± 0.8	14.5± 0.9
24.7 ppm	14.0± 0.8	15.0± 0.8	15.9± 0.5	15.7± 0.7	15.9± 0.4	15.8± 0.6	15.3± 1.0
74.1 ppm	14.4± 0.8	15.8± 0.9**	15.9± 0.7	16.1± 0.5**	15.9± 0.7	15.7± 0.8	15.5± 0.7
222 ppm	13.9± 0.6	15.0± 0.6	16.2± 0.5	16.2± 0.6**	16.5± 0.5**	16.7± 0.7**	15.3± 3.9**
667 ppm	12.7± 0.4	14.7± 0.5	15.7± 0.7	16.0± 0.8*	16.2± 1.3	16.5± 1.0**	16.3± 0.9**
2000 ppm	8.6± 1.9**	12.3± 1.2**	13.2± 0.7**	14.1± 1.0*	14.1± 2.4	14.3± 1.6	14.9± 0.9

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0057
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration 8-7(7)	week-day(effective) 9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	14.1± 1.0	14.0± 1.0	13.8± 0.9	13.8± 1.0	13.7± 0.9	13.2± 1.1
24.7 ppm	15.4± 1.2	15.1± 1.1	15.5± 1.2**	15.4± 0.8**	15.3± 0.6**	14.6± 0.6**
74.1 ppm	15.6± 1.1*	14.7± 0.8	14.8± 0.7	14.9± 0.7*	15.0± 0.7*	14.5± 0.6*
222 ppm	16.6± 1.5**	16.1± 1.4**	15.7± 0.9**	15.7± 1.0**	16.2± 1.2**	15.5± 1.0**
667 ppm	16.4± 1.0**	15.8± 0.8**	16.3± 1.1**	16.1± 1.1**	16.2± 1.1**	15.4± 1.0**
2000 ppm	15.5± 1.2*	15.6± 1.5*	15.8± 1.1**	15.8± 1.2**	16.1± 1.3**	15.4± 1.4**

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

APPENDIX C 3-2

FOOD CONSUMPTION CHANGES (THIRTEEN-WEEK STUDIES: SUMMARY)

RAT: FEMALE

STUDY NO. : 0057
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	10.7± 0.7	10.5± 0.6	10.8± 1.4	10.3± 0.9	10.3± 0.9	10.4± 1.3	10.1± 1.2
24.7 ppm	11.1± 0.7	10.7± 0.6	10.9± 0.6	10.6± 0.7	11.0± 1.0	10.9± 0.7	11.4± 1.4
74.1 ppm	11.1± 0.8	10.9± 0.5	11.5± 1.3	10.9± 0.5	11.4± 0.5*	12.3± 2.6*	11.2± 0.9
222 ppm	10.6± 0.6	10.5± 0.8	11.0± 0.7	10.6± 0.9	11.6± 1.2*	11.0± 0.8	11.3± 1.1
667 ppm	9.5± 0.5**	10.5± 0.6	10.7± 0.8	10.8± 0.6	10.8± 1.0	11.3± 0.9	11.0± 1.0
2000 ppm	6.4± 0.4**	9.4± 0.7**	9.7± 1.5	10.9± 2.5	10.8± 1.8	10.6± 1.5	11.1± 2.0

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0057
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	9.7± 1.2	10.4± 3.1	10.2± 2.6	10.2± 2.3	10.3± 2.3	9.8± 2.6
24.7 ppm	11.0± 1.2	11.3± 1.3	11.1± 0.6	11.7± 2.5	11.4± 3.0	10.0± 0.9
74.1 ppm	11.4± 1.0**	11.0± 0.7	11.7± 2.9	11.2± 1.4	10.7± 0.9	10.7± 1.2
222 ppm	12.1± 2.3**	11.3± 2.2	11.2± 1.4	10.8± 0.7	11.2± 1.2	10.6± 0.8
667 ppm	11.3± 1.3	11.2± 1.1	11.6± 1.3	11.5± 1.1	11.4± 1.1	11.7± 1.9**
2000 ppm	10.4± 0.7	11.4± 3.9	11.8± 3.8	12.5± 3.8	10.7± 1.1	11.5± 2.9

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX C 3-3

FOOD CONSUMPTION CHANGES (THIRTEEN-WEEK STUDIES: SUMMARY)

MOUSE: MALE

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	3.6± 0.5	4.2± 0.3	3.7± 0.3	3.5± 0.3	3.6± 0.3	3.5± 0.3	3.8± 0.4
74.1 ppm	3.8± 0.5	4.2± 0.5	3.9± 0.4	3.9± 0.5*	3.7± 0.4	3.7± 0.4	3.7± 0.4
222 ppm	4.0± 0.4	4.2± 0.2	3.9± 0.2	3.9± 0.3*	3.7± 0.2	4.0± 0.2**	3.9± 0.3
667 ppm	3.6± 0.3	4.1± 0.4	3.7± 0.2	3.9± 0.2	3.4± 0.3	3.7± 0.2	3.9± 0.4
2000 ppm	3.6± 0.4	3.7± 0.3	3.7± 0.2	3.8± 0.2	3.5± 0.3	3.7± 0.3	3.7± 0.2
6000 ppm	2.3± 0.2**	2.9± 0.6**	3.1± 0.6	3.1± 0.3**	2.8± 0.3**	3.1± 0.4*	3.4± 0.5

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	3.6± 0.4	3.6± 0.3	3.6± 0.4	3.3± 0.4	4.0± 0.5	3.5± 0.3
74.1 ppm	3.9± 0.4	3.8± 0.3	4.2± 0.5*	3.6± 0.7	4.3± 0.5	3.5± 0.4
222 ppm	4.0± 0.3*	3.9± 0.2	4.1± 0.4*	3.5± 0.5	4.3± 0.3	3.9± 0.3
667 ppm	3.8± 0.2	3.7± 0.2	4.1± 0.4	3.4± 0.2	4.2± 0.4	4.1± 0.3**
2000 ppm	3.8± 0.3	3.8± 0.1	4.0± 0.4	3.5± 0.5	4.2± 0.3	4.0± 0.4*
6000 ppm	3.3± 0.4	3.3± 0.4*	3.2± 0.4	3.3± 0.3	3.4± 0.4**	3.4± 0.6

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

APPENDIX C 3-4

FOOD CONSUMPTION CHANGES (THIRTEEN-WEEK STUDIES: SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	3.4± 0.2	3.8± 0.2	3.8± 0.4	3.6± 0.4	3.5± 0.4	3.8± 0.4	3.8± 0.3
74.1 ppm	3.5± 0.2	3.9± 0.3	3.9± 0.3	3.7± 0.3	3.6± 0.3	3.9± 0.3	4.0± 0.2
222 ppm	3.8± 0.3*	4.0± 0.3	4.1± 0.3	3.7± 0.3	3.7± 0.5	4.2± 0.5	4.0± 0.2
667 ppm	3.7± 0.3	4.0± 0.5	3.9± 0.3	4.2± 0.6	3.7± 0.3	4.1± 0.3	4.2± 0.3
2000 ppm	3.2± 0.2	3.6± 0.2	3.7± 0.2	3.6± 0.4	3.6± 0.3	3.6± 0.3	3.9± 0.5
6000 ppm	3.1± 1.1	3.9± 1.3	3.1± 0.6**	2.9± 0.8	2.5± 0.4**	2.9± 0.7	3.0± 0.8

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

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	3.8± 0.2	4.1± 0.3	4.3± 0.3	3.5± 0.3	4.6± 0.3	4.0± 0.4
74.1 ppm	4.0± 0.3	4.4± 0.4	4.4± 0.4	3.7± 0.5	4.8± 0.3	4.2± 0.6
222 ppm	4.1± 0.3	4.2± 0.4	4.8± 0.9	3.8± 0.4	4.8± 0.5	4.5± 0.6
667 ppm	4.1± 0.2	4.5± 0.4	4.5± 0.3	3.9± 0.4	5.0± 0.5	4.6± 0.4
2000 ppm	3.8± 0.4	4.0± 0.4	4.0± 0.4	3.7± 0.4	4.0± 0.3	4.1± 0.4
6000 ppm	3.3± 0.8	3.9± 1.1	3.3± 0.8*	3.6± 0.7	3.9± 1.0	3.9± 1.1

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

APPENDIX C 4-1

CHEMICAL INTAKE CHANGES (THIRTEEN-WEEK STUDIES: SUMMARY)

RAT: MALE

STUDY NO. : 0057
ANIMAL : RAT F344
UNIT : mg／kg／d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
24.7 ppm	0.210± 0.007	0.187± 0.004	0.173± 0.004	0.158± 0.006	0.148± 0.005	0.139± 0.003	0.129± 0.005
74.1 ppm	0.641± 0.020	0.581± 0.018	0.516± 0.012	0.483± 0.009	0.444± 0.019	0.416± 0.018	0.393± 0.014
222 ppm	1.880± 0.036	1.680± 0.032	1.577± 0.037	1.454± 0.037	1.366± 0.046	1.310± 0.043	1.156± 0.251
667 ppm	5.341± 0.198	5.070± 0.110	4.732± 0.086	4.399± 0.126	4.118± 0.187	3.975± 0.125	3.762± 0.161
2000 ppm	12.774± 1.619	15.383± 1.129	14.300± 1.659	13.385± 0.476	12.539± 0.515	11.830± 0.553	11.569± 1.116

STUDY NO. : 0057
ANIMAL : RAT F344
UNIT : mg／kg／d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
24.7 ppm	0.125± 0.007	0.118± 0.006	0.118± 0.006	0.114± 0.004	0.111± 0.004	0.104± 0.003
74.1 ppm	0.383± 0.029	0.352± 0.015	0.344± 0.014	0.339± 0.014	0.335± 0.014	0.317± 0.012
222 ppm	1.212± 0.128	1.132± 0.090	1.076± 0.041	1.045± 0.042	1.055± 0.062	0.984± 0.045
667 ppm	3.646± 0.229	3.374± 0.117	3.374± 0.189	3.245± 0.200	3.200± 0.167	2.997± 0.173
2000 ppm	11.430± 1.061	10.940± 1.059	10.640± 0.792	10.345± 0.853	10.230± 0.742	9.763± 1.040

APPENDIX C 4-2

CHEMICAL INTAKE CHANGES (THIRTEEN-WEEK STUDIES: SUMMARY)

RAT: FEMALE

STUDY NO. : 0057
ANIMAL : RAT F344
UNIT : mg／kg／d a y
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
24.7 ppm	0.231± 0.009	0.200± 0.005	0.187± 0.007	0.172± 0.006	0.168± 0.012	0.160± 0.006	0.162± 0.026
74.1 ppm	0.702± 0.056	0.616± 0.014	0.601± 0.053	0.539± 0.021	0.528± 0.020	0.545± 0.127	0.479± 0.024
222 ppm	2.046± 0.077	1.810± 0.144	1.741± 0.105	1.602± 0.085	1.637± 0.207	1.480± 0.075	1.473± 0.072
667 ppm	5.610± 0.253	5.535± 0.274	5.130± 0.279	4.865± 0.201	4.619± 0.263	4.553± 0.230	4.314± 0.213
2000 ppm	12.881± 0.909	16.373± 0.871	15.207± 1.575	16.101± 3.714	14.833± 2.134	13.921± 1.527	14.134± 2.405

STUDY NO. : 0057
ANIMAL : RAT F344
UNIT : mg/kg/day
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
24.7 ppm	0.152± 0.020	0.153± 0.022	0.148± 0.012	0.153± 0.040	0.147± 0.045	0.129± 0.016
74.1 ppm	0.472± 0.033	0.448± 0.022	0.467± 0.118	0.439± 0.052	0.413± 0.023	0.412± 0.044
222 ppm	1.513± 0.264	1.407± 0.323	1.356± 0.211	1.285± 0.046	1.305± 0.125	1.224± 0.041
667 ppm	4.296± 0.377	4.118± 0.218	4.184± 0.434	4.121± 0.395	3.978± 0.236	4.060± 0.617
2000 ppm	12.734± 0.673	13.916± 5.259	13.828± 4.093	14.584± 4.550	12.073± 0.874	12.941± 3.055

APPENDIX C 4-3

CHEMICAL INTAKE CHANGES (THIRTEEN-WEEK STUDIES: SUMMARY)

MOUSE: MALE

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
UNIT : mg／kg／d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
74.1 ppm	1.206± 0.121	1.209± 0.120	1.075± 0.092	1.060± 0.103	0.979± 0.089	0.962± 0.076	0.945± 0.095
222 ppm	3.777± 0.276	3.736± 0.275	3.359± 0.167	3.217± 0.197	2.983± 0.174	3.080± 0.160	2.954± 0.135
667 ppm	10.507± 0.631	10.865± 0.703	9.597± 0.731	9.455± 0.738	8.285± 0.926	8.649± 0.749	8.934± 1.036
2000 ppm	30.949± 2.762	30.185± 1.573	29.657± 1.478	28.946± 1.680	26.546± 2.028	27.221± 2.373	26.761± 1.839
6000 ppm	69.026± 9.156	86.493± 17.356	87.331± 15.626	81.567± 7.205	73.338± 3.736	77.996± 12.500	80.987± 15.161

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
UNIT : mg/kg/d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
74.1 ppm	0.935± 0.092	0.906± 0.062	0.960± 0.111	0.822± 0.102	0.946± 0.123	0.761± 0.082
222 ppm	2.879± 0.192	2.795± 0.183	2.808± 0.181	2.407± 0.324	2.852± 0.144	2.504± 0.211
667 ppm	8.319± 0.649	8.085± 0.769	8.493± 0.993	7.106± 0.744	8.460± 1.055	7.817± 0.823
2000 ppm	26.258± 1.931	26.119± 1.376	26.419± 2.473	23.465± 2.555	26.521± 2.224	24.821± 1.837
6000 ppm	74.946± 9.180	73.801± 5.844	70.838± 6.900	70.803± 4.810	72.982± 7.357	72.135± 11.773

APPENDIX C 4-4

CHEMICAL INTAKE CHANGES (THIRTEEN-WEEK STUDIES: SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
UNIT : mg/kg/day
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
74.1 ppm	1.356± 0.067	1.443± 0.098	1.431± 0.074	1.361± 0.093	1.262± 0.086	1.318± 0.085	1.305± 0.064
222 ppm	4.241± 0.371	4.431± 0.450	4.376± 0.419	4.078± 0.362	3.892± 0.514	4.096± 0.365	3.867± 0.245
667 ppm	12.564± 1.255	13.165± 1.568	13.013± 0.892	13.256± 1.237	11.314± 0.865	12.066± 0.657	11.982± 0.621
2000 ppm	32.288± 1.589	35.940± 2.814	36.214± 2.674	34.816± 2.441	31.891± 2.234	31.191± 2.607	33.367± 4.120
6000 ppm	117.957± 43.418	136.719± 49.326	102.833± 21.802	91.513± 25.029	75.598± 11.437	86.662± 19.380	87.264± 22.149

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
UNIT : mg/kg/day
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
74.1 ppm	1.272± 0.065	1.364± 0.130	1.333± 0.096	1.156± 0.146	1.378± 0.099	1.198± 0.160
222 ppm	3.895± 0.409	4.212± 0.910	4.251± 0.832	3.446± 0.416	4.129± 0.461	3.821± 0.430
667 ppm	11.655± 0.555	12.556± 0.768	12.121± 0.561	10.896± 0.624	12.789± 0.682	11.655± 0.766
2000 ppm	32.255± 2.196	33.176± 2.097	31.897± 2.604	29.877± 1.697	31.526± 2.157	31.491± 2.125
6000 ppm	93.467± 20.952	109.571± 28.731	88.899± 20.701	95.174± 18.482	101.936± 26.046	101.172± 28.347

APPENDIX C 5-1

HEMATOLOGY (THIRTEEN-WEEK STUDIES: SUMMARY)

RAT: MALE

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	PLATELET $10^3/\mu\ell$
Control	10	9.45± 0.29	16.0± 0.5	43.3± 1.5	45.8± 0.4	753± 47
24.7 ppm	10	9.31± 0.29	15.7± 0.2	42.8± 1.4	46.0± 0.2	829± 43**
74.1 ppm	10	8.90± 0.28**	15.3± 0.3**	41.7± 1.4*	46.9± 0.4	826± 44**
222 ppm	10	8.36± 0.25**	14.8± 0.4**	40.8± 1.3**	48.8± 0.6**	748± 42
667 ppm	10	7.18± 0.20**	14.3± 0.2**	39.4± 1.0**	54.9± 1.3**	530± 42**
2000 ppm	10	5.42± 0.20**	14.2± 0.4**	40.7± 1.4**	75.2± 2.3**	435± 35**

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

(HCL070)

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$		Differential WBC (%) N-BAND		N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	10	3.34±	0.73	0±	0	19±	5	1±	0	0±	0	3±	1	77±	5	0±	0
24.7 ppm	10	3.68±	1.35	0±	0	19±	4	1±	1	0±	0	3±	1	77±	4	0±	0
74.1 ppm	10	3.62±	0.78	0±	0	17±	3	1±	1	0±	0	3±	1	79±	4	0±	0
222 ppm	10	3.28±	0.53	0±	0	17±	4	1±	0	0±	0	3±	1	79±	4	0±	0
667 ppm	10	3.17±	0.49	0±	0	15±	4	1±	1	0±	0	4±	2	80±	6	0±	1
2000 ppm	10	13.98±	3.18**	0±	0	10±	3**	1±	1	0±	0	4±	1	84±	4**	1±	1

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

APPENDIX C 5-2

HEMATOLOGY (THIRTEEN-WEEK STUDIES: SUMMARY)

RAT: FEMALE

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	PLATELET $10^3/\mu\ell$
Control	09	8.75± 0.38	15.9± 0.6	42.7± 1.8	48.8± 0.3	795± 81
24.7 ppm	10	8.42± 0.34*	15.6± 0.5	41.8± 1.6	49.6± 0.2	839± 57
74.1 ppm	10	7.94± 0.16**	15.0± 0.3	40.5± 1.0	51.0± 0.4	849± 41
222 ppm	10	7.29± 0.22**	14.3± 0.4**	38.8± 1.1**	53.3± 0.5**	798± 73
667 ppm	10	5.93± 0.18**	13.9± 0.3**	36.4± 4.3**	61.2± 6.4**	559± 30**
2000 ppm	10	4.58± 0.26**	13.8± 0.2**	40.6± 1.1	88.8± 4.3**	497± 48**

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

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$		Differential WBC (%) N-BAND		N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	09	2.86±	0.94	0±	0	16±	6	1±	1	0±	0	3±	1	80±	7	0±	0
24.7 ppm	10	2.57±	0.80	0±	0	16±	5	1±	0	0±	0	4±	1	79±	5	0±	0
74.1 ppm	10	2.68±	0.50	0±	0	16±	5	1±	1	0±	0	3±	1	80±	5	0±	0
222 ppm	10	3.43±	1.08	0±	0	15±	5	1±	1	0±	0	4±	1	80±	6	0±	0
667 ppm	10	3.97±	0.70	0±	0	14±	2	1±	1	0±	0	4±	2	82±	3	0±	0
2000 ppm	10	42.80±	18.85**	0±	0	8±	2**	0±	1	0±	0	3±	1	88±	3**	0±	0

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX C 5-3

HEMATOLOGY (THIRTEEN-WEEK STUDIES: SUMMARY)

MOUSE: MALE

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV fℓ	PLATELET $10^3/\mu\ell$
Control	10	10.68± 0.33	15.0± 0.3	44.0± 1.2	41.2± 0.5	1321± 71
74.1 ppm	08	10.55± 0.35	14.8± 0.4	43.3± 1.6	41.0± 0.5	1385± 107
222 ppm	08	10.64± 0.30	14.9± 0.4	43.7± 1.0	41.0± 0.5	1323± 70
667 ppm	10	10.34± 0.47	14.9± 0.4	43.4± 1.7	42.0± 0.7	1364± 106
2000 ppm	10	9.12± 0.28**	16.3± 0.8*	39.2± 1.3**	42.9± 0.4**	1296± 59
6000 ppm	09	6.58± 0.92**	12.7± 1.1**	38.8± 3.9**	59.3± 3.7**	922± 57**

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

(HCL070)

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$		Differential WBC (%) N-BAND		N-SEG		EOSINO		BASO	MONO		LYMPHO		OTHER	
Control	10	1.84±	1.03	0±	0	14±	3	1±	1	-	2±	0	83±	2	0±	0
74.1 ppm	08	1.29±	0.62	0±	0	14±	4	1±	1	-	2±	1	83±	5	0±	0
222 ppm	08	1.39±	0.40	0±	0	16±	4	1±	1	-	2±	1	82±	4	0±	0
667 ppm	10	1.71±	0.88	0±	0	12±	3	1±	1	-	2±	1	85±	4	0±	0
2000 ppm	10	12.34±	8.63*	0±	0	11±	2	1±	1	-	2±	1	86±	2	0±	0
6000 ppm	09	56.51±	25.63**	0±	0	13±	4	0±	1	-	4±	1**	83±	4	0±	0

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

APPENDIX C 5-4

HEMATOLOGY (THIRTEEN-WEEK STUDIES: SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV fℓ	PLATELET $10^3/\mu\ell$
Control	10	10.42± 0.34	14.9± 0.4	43.4± 1.4	41.6± 0.4	1094± 144
74.1 ppm	10	10.51± 0.47	15.1± 0.6	44.0± 2.2	41.8± 0.5	1208± 94
222 ppm	10	10.40± 0.44	14.9± 0.5	43.7± 1.7	42.0± 0.3	1194± 112
667 ppm	10	9.83± 0.38*	15.0± 0.4	42.2± 1.8	42.9± 0.5**	1207± 190
2000 ppm	10	8.69± 0.30**	15.8± 0.7**	37.6± 1.5**	43.2± 0.8**	1123± 113
6000 ppm	09	6.18± 0.54**	12.1± 0.8**	36.8± 3.6**	59.5± 2.2**	788± 166**

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

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$		Differential WBC (%) N-BAND		N-SEG		EOSINO		BASO	MONO		LYMPHO		OTHER	
Control	10	1.32±	0.45	0±	0	13±	4	1±	0	-	2±	1	84±	4	0±	0
74.1 ppm	10	1.89±	1.39	0±	0	15±	6	1±	1	-	2±	1	82±	6	0±	0
222 ppm	10	1.54±	0.88	0±	0	16±	5	1±	1	-	2±	1	81±	5	0±	0
667 ppm	10	1.63±	0.53	0±	1	10±	3	1±	1	-	2±	1	87±	3	0±	0
2000 ppm	10	17.91±	6.98**	0±	0	9±	3	1±	1	-	3±	1	87±	4	0±	0
6000 ppm	09	57.21±	13.43**	0±	0	8±	2*	1±	1	-	4±	2*	87±	3	0±	0

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX C 6-1

BIOCHEMISTRY (THIRTEEN-WEEK STUDIES: SUMMARY)

RAT: MALE

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	TOTAL PROTEIN g/dℓ		ALBUMIN g/dℓ		A/G RATIO		T-BILIRUBIN mg/dℓ		GLUCOSE mg/dℓ		T-CHOLESTEROL mg/dℓ		TRIGLYCERIDE mg/dℓ	
Control	10	6.5±	0.2	3.7±	0.1	1.3±	0.1	0.15±	0.02	191±	10	55±	5	89±	23
24.7 ppm	10	6.6±	0.1	3.8±	0.1	1.3±	0.0	0.14±	0.02	200±	16	54±	3	93±	26
74.1 ppm	10	6.5±	0.1	3.7±	0.1	1.3±	0.1	0.14±	0.01	200±	13	54±	4	99±	19
222 ppm	10	6.5±	0.2	3.7±	0.1	1.3±	0.1	0.16±	0.02	197±	20	53±	3	92±	24
667 ppm	10	6.1±	0.1**	3.5±	0.1**	1.4±	0.1	0.23±	0.03*	191±	14	50±	3	83±	11
2000 ppm	10	6.2±	0.1**	3.6±	0.1	1.4±	0.1	0.47±	0.06**	176±	20	63±	6*	66±	15

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

(HCL074)

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	GOT IU/ℓ		GPT IU/ℓ		LDH IU/ℓ		ALP IU/ℓ		LAP IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ	
Control	10	64±	8	21±	2	189±	45	230±	15	54±	2	110±	18	17.2±	1.3
24.7 ppm	10	65±	10	22±	3	213±	41	235±	12	53±	2	118±	20	17.2±	1.1
74.1 ppm	10	65±	9	22±	2	196±	30	226±	15	53±	1	108±	13	16.9±	1.1
222 ppm	10	64±	12	20±	4	186±	27	211±	12	50±	1**	111±	17	16.8±	1.7
667 ppm	10	60±	8	16±	2**	163±	18	204±	58**	47±	2**	94±	12	17.3±	1.4
2000 ppm	10	77±	13*	17±	2*	249±	68	180±	19**	46±	1**	104±	18	19.4±	2.0**

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

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	CREATININE mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	10	0.5± 0.1	142± 1	3.2± 0.1	104± 2	10.5± 0.2	4.9± 0.6
24.7 ppm	10	0.5± 0.1	142± 1	3.2± 0.1	103± 1	10.6± 0.2	4.9± 0.7
74.1 ppm	10	0.5± 0.0	141± 1	3.1± 0.2	103± 1	10.5± 0.2	4.7± 0.5
222 ppm	10	0.5± 0.1	141± 2	3.3± 0.2	103± 1	10.5± 0.2	5.3± 0.7
667 ppm	10	0.5± 0.1	141± 1	3.3± 0.3	104± 2	10.4± 0.2	5.6± 0.4*
2000 ppm	10	0.5± 0.1	141± 1	3.2± 0.3	102± 1	10.5± 0.2	6.4± 0.5**

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

APPENDIX C 6-2

BIOCHEMISTRY (THIRTEEN-WEEK STUDIES: SUMMARY)

RAT: FEMALE

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	TOTAL PROTEIN g／dℓ	ALBUMIN g／dℓ	A/G RATIO	T-BILIRUBIN mg／dℓ	GLUCOSE mg／dℓ	T-CHOLESTEROL mg／dℓ	TRIGLYCERIDE mg／dℓ
Control	09	6.3± 0.3	3.6± 0.2	1.3± 0.1	0.19± 0.02	147± 22	73± 9	41± 9
24.7 ppm	10	6.5± 0.2	3.7± 0.1	1.4± 0.1	0.20± 0.04	148± 12	79± 5	45± 6
74.1 ppm	10	6.4± 0.3	3.7± 0.1	1.4± 0.1	0.19± 0.04	157± 8	78± 7	41± 6
222 ppm	10	6.3± 0.2	3.7± 0.1	1.4± 0.1	0.23± 0.02	152± 14	77± 7	42± 7
667 ppm	10	6.2± 0.2	3.7± 0.2	1.5± 0.1**	0.36± 0.06**	160± 20	74± 7	37± 7
2000 ppm	10	6.1± 0.2	3.7± 0.1	1.5± 0.1**	0.58± 0.05**	151± 15	80± 4	36± 9

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

(HCL074)

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	GOT IU/ℓ	GPT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	LAP IU/ℓ	CPK IU/ℓ	UREA NITROGEN mg/dℓ
Control	09	58± 4	18± 3	215± 81	170± 17	55± 3	110± 26	17.3± 2.3
24.7 ppm	10	65± 11	22± 6	233± 60	162± 14	53± 2	123± 36	17.1± 1.8
74.1 ppm	10	62± 9	21± 6	226± 64	159± 13	53± 3	108± 19	17.6± 2.8
222 ppm	10	60± 5	18± 4	188± 45	151± 12*	50± 2**	104± 16	18.6± 2.2
667 ppm	10	61± 11	15± 3	183± 68	132± 18**	46± 2**	96± 20	18.8± 2.0
2000 ppm	10	67± 4	13± 1**	225± 43	136± 17**	45± 1**	101± 23	21.1± 1.8**

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

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	CREATININE mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	09	0.5± 0.1	141± 1	3.1± 0.2	106± 2	10.3± 0.3	4.6± 1.3
24.7 ppm	10	0.5± 0.1	140± 1	3.2± 0.3	106± 1	10.5± 0.2	4.5± 1.1
74.1 ppm	10	0.4± 0.1	140± 1	3.2± 0.2	105± 2	10.3± 0.3	4.5± 0.6
222 ppm	10	0.5± 0.1	140± 1	3.2± 0.2	105± 1	10.3± 0.3	4.8± 0.8
667 ppm	10	0.5± 0.1	141± 1	3.1± 0.2	105± 1	10.2± 0.2	4.8± 0.9
2000 ppm	10	0.4± 0.1	141± 1	3.1± 0.7	105± 1	10.1± 0.2	5.6± 0.7

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

APPENDIX C 6-3

BIOCHEMISTRY (THIRTEEN-WEEK STUDIES: SUMMARY)

MOUSE: MALE

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	TOTAL PROTEIN g／dℓ	ALBUMIN g／dℓ	A/G RATIO	T-BILIRUBIN mg／dℓ	GLUCOSE mg／dℓ	T-CHOLESTEROL mg／dℓ	GOT IU／ℓ
Control	10	5.0± 0.1	2.9± 0.1	1.4± 0.1	0.28± 0.03	211± 48	87± 8	36± 3
74.1 ppm	08	5.0± 0.2	2.8± 0.1	1.3± 0.1	0.31± 0.04	238± 25	82± 9	37± 4
222 ppm	08	5.1± 0.2	2.9± 0.1	1.3± 0.1	0.27± 0.05	246± 33	94± 10	36± 5
667 ppm	10	5.0± 0.2	2.9± 0.1	1.3± 0.0	0.29± 0.04	261± 32**	95± 5	40± 7
2000 ppm	10	4.9± 0.2	2.8± 0.1	1.4± 0.1	0.30± 0.13	246± 27	96± 9	38± 7
6000 ppm	10	5.2± 0.2*	3.0± 0.1	1.4± 0.1	0.46± 0.05**	234± 20	112± 5**	134± 71**

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	GPT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	LAP IU/ℓ	UREA NITROGEN mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ
Control	10	9± 2	294± 47	145± 5	41± 1	26.5± 2.6	151± 2	4.2± 0.3
74.1 ppm	08	9± 1	361± 119	145± 6	42± 3	26.0± 2.4	150± 2	4.3± 0.2
222 ppm	08	10± 2	335± 85	148± 9	43± 2	24.7± 3.2	151± 1	4.4± 0.4
667 ppm	10	11± 5	351± 108	150± 7	43± 2	25.9± 3.0	151± 2	4.4± 0.5
2000 ppm	10	9± 2	434± 226	138± 7	37± 3**	29.0± 5.0	149± 2	4.4± 0.3
6000 ppm	10	54± 46**	956± 322**	193± 21**	47± 3**	31.3± 2.4**	151± 2	4.2± 0.6

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

(HCL074)

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	CHLORIDE mEq/ℓ
Control	10	122± 2
74.1 ppm	08	121± 1
222 ppm	08	121± 2
667 ppm	10	120± 3
2000 ppm	10	120± 2
6000 ppm	10	121± 1

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

APPENDIX C 6-4

BIOCHEMISTRY (THIRTEEN-WEEK STUDIES: SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	TOTAL PROTEIN g／dℓ	ALBUMIN g／dℓ	A/G RATIO	T-BILIRUBIN mg／dℓ	GLUCOSE mg／dℓ	T-CHOLESTEROL mg／dℓ	GOT I U／ℓ
Control	10	5.0± 0.2	2.9± 0.1	1.4± 0.1	0.32± 0.03	166± 21	75± 6	48± 8
74.1 ppm	10	5.0± 0.2	3.0± 0.1	1.4± 0.1	0.33± 0.06	164± 27	77± 6	47± 9
222 ppm	10	5.0± 0.2	2.9± 0.1	1.4± 0.1	0.33± 0.07	164± 25	77± 8	50± 9
667 ppm	10	4.9± 0.2	2.9± 0.1	1.4± 0.1	0.29± 0.04	182± 22	81± 7	46± 9
2000 ppm	10	5.0± 0.2	2.9± 0.1	1.4± 0.1	0.30± 0.05	185± 25	95± 7**	50± 8
6000 ppm	09	5.2± 0.2*	3.0± 0.1	1.3± 0.1	0.50± 0.10**	209± 25**	115± 11**	79± 15**

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

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	GPT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	LAP IU/ℓ	UREA NITROGEN mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ
Control	10	11± 2	375± 80	216± 22	43± 5	18.5± 3.6	151± 2	4.4± 0.4
74.1 ppm	10	11± 2	466± 76	215± 20	40± 2	19.1± 2.1	151± 3	4.3± 0.6
222 ppm	10	11± 2	431± 132	212± 22	41± 3	17.8± 2.7	151± 2	4.3± 0.5
667 ppm	10	11± 2	372± 106	201± 14	40± 4	20.0± 5.2	151± 2	4.5± 0.5
2000 ppm	10	12± 2	460± 87	202± 26	37± 3**	23.1± 2.1*	151± 2	4.5± 0.3
6000 ppm	09	17± 2**	981± 593**	216± 31	48± 3*	31.1± 5.8**	151± 2	4.7± 0.8

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

(HCL074)

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	CHLORIDE mEq/ℓ
Control	10	121± 2
74.1 ppm	10	120± 3
222 ppm	10	120± 2
667 ppm	10	121± 2
2000 ppm	10	121± 1
6000 ppm	09	120± 3

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

APPENDIX C 7-1

URINALYSIS (THIRTEEN-WEEK STUDIES: SUMMARY)

RAT: MALE

STUDY NO. : 0057
ANIMAL : RAT F344
SAMPLING DATE : 013-7
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	+	2+	3+	CHI	Bilirubin −	+	2+	3+	CHI
Control	10	0	0	0	0	1	9	0		0	0	4	6	0	0		10	0	0	0	0	0		10	0	0	0		10	0	0	0	
24.7 ppm	10	0	0	0	0	0	10	0		0	0	2	8	0	0		10	0	0	0	0	0		10	0	0	0		10	0	0	0	
74.1 ppm	10	0	0	0	0	0	10	0		0	0	1	9	0	0		10	0	0	0	0	0		10	0	0	0		10	0	0	0	
222 ppm	10	0	0	0	0	0	9	1		0	0	2	8	0	0		10	0	0	0	0	0		10	0	0	0		10	0	0	0	
667 ppm	10	0	0	0	0	0	10	0		0	0	4	6	0	0		10	0	0	0	0	0		10	0	0	0		10	0	0	0	
2000 ppm	10	0	0	1	1	4	4	0		0	0	3	7	0	0		10	0	0	0	0	0		8	2	0	0		10	0	0	0	

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

STUDY NO. : 0057 URINALYSIS
ANIMAL : RAT F344
SAMPLING DATE : 013-7
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0		10	0	0	0	0	
24.7 ppm	10	10	0	0	0	0		10	0	0	0	0	
74.1 ppm	10	10	0	0	0	0		10	0	0	0	0	
222 ppm	10	10	0	0	0	0		10	0	0	0	0	
667 ppm	10	10	0	0	0	0		10	0	0	0	0	
2000 ppm	10	10	0	0	0	0		10	0	0	0	0	

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

APPENDIX C 7-2

URINALYSIS (THIRTEEN-WEEK STUDIES: SUMMARY)

RAT: FEMALE

STUDY NO. : 0057
ANIMAL : RAT F344
SAMPLING DATE : 013-7
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	+	2+	3+	CHI	Bilirubin −	+	2+	3+	CHI
Control	10	0	0	0	0	6	4	0		0	0	8	2	0	0		10	0	0	0	0	0		7	3	0	0		10	0	0	0	
24.7 ppm	10	0	0	0	1	5	4	0		0	0	8	2	0	0		10	0	0	0	0	0		9	1	0	0		10	0	0	0	
74.1 ppm	10	0	0	0	2	6	2	0		0	0	8	2	0	0		10	0	0	0	0	0		6	4	0	0		10	0	0	0	
222 ppm	10	0	0	0	3	4	3	0		0	0	8	2	0	0		10	0	0	0	0	0		8	2	0	0		10	0	0	0	
667 ppm	10	0	0	0	1	3	6	0		0	0	10	0	0	0		10	0	0	0	0	0		9	1	0	0		10	0	0	0	
2000 ppm	10	0	0	1	0	5	4	0		0	0	6	4	0	0		10	0	0	0	0	0		9	1	0	0		10	0	0	0	

Significent difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

STUDY NO. : 0057 URINALYSIS
ANIMAL : RAT F344
SAMPLING DATE : 013-7
SEX : FEMALE REPORT TYPE : A1

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0		10	0	0	0	0	
24.7 ppm	10	10	0	0	0	0		10	0	0	0	0	
74.1 ppm	10	10	0	0	0	0		10	0	0	0	0	
222 ppm	10	10	0	0	0	0		10	0	0	0	0	
667 ppm	10	10	0	0	0	0		10	0	0	0	0	
2000 ppm	10	10	0	0	0	0		10	0	0	0	0	

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

APPENDIX C 7-3

URINALYSIS (THIRTEEN-WEEK STUDIES: SUMMARY)

MOUSE: MALE

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-7
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	+	2+	3+	CHI	Occult blood −	±	+	2+	3+	CHI
Control	10	0	0	4	3	2	1	0		0	2	6	2	0	0		10	0	0	0	0	0		9	1	0	0		10	0	0	0	0	
74.1 ppm	9	0	0	1	3	2	3	0		0	0	8	1	0	0		9	0	0	0	0	0		7	2	0	0		9	0	0	0	0	
222 ppm	10	0	2	1	0	1	6	0	*	0	2	8	0	0	0		10	0	0	0	0	0		8	2	0	0		10	0	0	0	0	
667 ppm	10	0	0	0	2	6	2	0		0	1	9	0	0	0		10	0	0	0	0	0		9	1	0	0		10	0	0	0	0	
2000 ppm	10	0	9	0	0	1	0	0	**	0	9	1	0	0	0	**	10	0	0	0	0	0		8	2	0	0		10	0	0	0	0	
6000 ppm	10	0	8	1	1	0	0	0	**	0	10	0	0	0	0	**	10	0	0	0	0	0		9	1	0	0		10	0	0	0	0	

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

STUDY NO. : 0058 URINALYSIS
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-7
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
74.1 ppm	9	9	0	0	0	0	
222 ppm	10	10	0	0	0	0	
667 ppm	10	10	0	0	0	0	
2000 ppm	10	10	0	0	0	0	
6000 ppm	10	10	0	0	0	0	

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

APPENDIX C 7-4

URINALYSIS (THIRTEEN-WEEK STUDIES: SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0058 URINALYSIS
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-7
SEX : FEMALE REPORT TYPE : A1

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	+	2+	3+	CHI	Occult blood −	±	+	2+	3+	CHI
Control	10	0	0	1	4	3	2	0		0	0	1	9	0	0		10	0	0	0	0	0		3	7	0	0		10	0	0	0	0	
74.1 ppm	10	0	0	3	4	3	0	0		0	0	1	9	0	0		10	0	0	0	0	0		6	4	0	0		10	0	0	0	0	
222 ppm	10	0	0	1	6	3	0	0		0	0	4	6	0	0		10	0	0	0	0	0		2	8	0	0		10	0	0	0	0	
667 ppm	10	0	1	4	2	3	0	0		0	0	4	5	1	0		10	0	0	0	0	0		5	5	0	0		10	0	0	0	0	
2000 ppm	10	0	1	7	2	0	0	0	*	0	0	7	3	0	0	**	8	2	0	0	0	0		3	7	0	0		10	0	0	0	0	
6000 ppm	9	0	3	4	0	2	0	0	*	0	2	5	2	0	0	*	7	2	0	0	0	0		3	6	0	0		9	0	0	0	0	

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

STUDY NO. : 0058 URINALYSIS
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-7
SEX : FEMALE REPORT TYPE : A1

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
74.1 ppm	10	10	0	0	0	0	
222 ppm	10	10	0	0	0	0	
667 ppm	10	10	0	0	0	0	
2000 ppm	10	10	0	0	0	0	
6000 ppm	9	9	0	0	0	0	

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

APPENDIX C 8-1

GROSS FINDINGS (THIRTEEN-WEEK STUDIES: SUMMARY)

RAT: MALE: SACRIFICED ANIMALS

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	24.7 ppm 10 (%)	74.1 ppm 10 (%)	222 ppm 10 (%)
subcutis	black		0 (0)	0 (0)	0 (0)	0 (0)
lymph node	enlarged		0 (0)	0 (0)	0 (0)	0 (0)
spleen	enlarged		0 (0)	0 (0)	3 (30)	8 (80)
	brown		0 (0)	0 (0)	1 (10)	0 (0)
	black		0 (0)	1 (10)	6 (60)	8 (80)
	granular		0 (0)	0 (0)	0 (0)	9 (90)
liver	enlarged		0 (0)	0 (0)	1 (10)	0 (0)
	brown		0 (0)	0 (0)	0 (0)	0 (0)
	black		0 (0)	0 (0)	0 (0)	0 (0)
	herniation		0 (0)	0 (0)	0 (0)	0 (0)
kidney	green		0 (0)	0 (0)	0 (0)	0 (0)
	black		0 (0)	0 (0)	3 (30)	4 (40)
urin bladd	nodule		0 (0)	0 (0)	1 (10)	0 (0)
testis	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
	nodule		0 (0)	0 (0)	0 (0)	1 (10)
other	blood:brown		0 (0)	0 (0)	0 (0)	0 (0)

Organ	Findings	Group Name NO. of Animals	667 ppm 10 (%)	2000 ppm 10 (%)
subcutis	black		0 (0)	1 (10)
lymph node	enlarged		1 (10)	0 (0)
spleen	enlarged		10 (100)	10 (100)
	brown		0 (0)	0 (0)
	black		10 (100)	10 (100)
	granular		10 (100)	1 (10)
liver	enlarged		0 (0)	2 (20)
	brown		3 (30)	7 (70)
	black		0 (0)	2 (20)
	herniation		1 (10)	0 (0)
kidney	green		3 (30)	1 (10)
	black		6 (60)	7 (70)
urin bladd	nodule		0 (0)	0 (0)
testis	atrophic		0 (0)	10 (100)
	nodule		0 (0)	0 (0)
other	blood:brown		0 (0)	1 (10)

APPENDIX C 8-2

GROSS FINDINGS (THIRTEEN-WEEK STUDIES: SUMMARY)

RAT: FEMALE: SACRIFICED ANIMALS

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	24.7 ppm 10 (%)	74.1 ppm 10 (%)	222 ppm 10 (%)
subcutis	brown		0 (0)	0 (0)	0 (0)	0 (0)
lung	brown		1 (10)	0 (0)	0 (0)	0 (0)
spleen	enlarged		0 (0)	0 (0)	3 (30)	6 (60)
	black		0 (0)	3 (30)	7 (70)	10 (100)
	granular		0 (0)	0 (0)	1 (10)	10 (100)
liver	red		1 (10)	0 (0)	0 (0)	0 (0)
	brown		0 (0)	0 (0)	0 (0)	0 (0)
	nodule		0 (0)	0 (0)	0 (0)	1 (10)
	herniation		1 (10)	0 (0)	0 (0)	0 (0)
kidney	green		0 (0)	0 (0)	0 (0)	4 (40)
	black		0 (0)	0 (0)	2 (20)	1 (10)
adrenal	nodule		1 (10)	0 (0)	0 (0)	0 (0)
	cyst		0 (0)	0 (0)	1 (10)	1 (10)
ovary	cyst		0 (0)	0 (0)	0 (0)	0 (0)
peritoneum	adhesion		0 (0)	0 (0)	0 (0)	1 (10)

Organ	Findings	Group Name NO. of Animals	667 ppm 10 (%)	2000 ppm 10 (%)
subcutis	brown		0 (0)	1 (10)
lung	brown		0 (0)	0 (0)
spleen	enlarged		8 (80)	10 (100)
	black		8 (80)	10 (100)
	granular		9 (90)	0 (0)
liver	red		0 (0)	2 (20)
	brown		2 (20)	6 (60)
	nodule		0 (0)	1 (10)
	herniation		0 (0)	0 (0)
kidney	green		1 (10)	0 (0)
	black		7 (70)	10 (100)
adrenal	nodule		0 (0)	0 (0)
	cyst		0 (0)	0 (0)
ovary	cyst		0 (0)	1 (10)
peritoneum	adhesion		0 (0)	0 (0)

APPENDIX C 8-3

GROSS FINDINGS (THIRTEEN-WEEK STUDIES: SUMMARY)

MOUSE: FEMALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 13W)

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	74.1 ppm 0 (%)	222 ppm 0 (%)	667 ppm 0 (%)
lung	red		- (-)	- (-)	- (-)	- (-)
spleen	enlarged		- (-)	- (-)	- (-)	- (-)
liver	green		- (-)	- (-)	- (-)	- (-)
kidney	brown		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 13W)

Organ	Findings	Group Name / NO. of Animals	2000 ppm 0 (%)	6000 ppm 1 (%)
lung	red		- (-)	1 (100)
spleen	enlarged		- (-)	1 (100)
liver	green		- (-)	1 (100)
kidney	brown		- (-)	1 (100)

APPENDIX C 8-4

GROSS FINDINGS (THIRTEEN-WEEK STUDIES: SUMMARY)

MOUSE: MALE: SACRIFICED ANIMALS

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	74.1 ppm 9 (%)	222 ppm 10 (%)	667 ppm 10 (%)
subcutis	black		0 (0)	0 (0)	0 (0)	0 (0)
	jaundice		0 (0)	0 (0)	0 (0)	0 (0)
lung	black		0 (0)	0 (0)	0 (0)	0 (0)
spleen	enlarged		0 (0)	0 (0)	0 (0)	0 (0)
	black		0 (0)	0 (0)	0 (0)	5 (50)
	black patch/zone		0 (0)	1 (11)	0 (0)	0 (0)
	black zone		1 (10)	1 (11)	1 (10)	0 (0)
liver	brown		0 (0)	0 (0)	0 (0)	0 (0)
	black		0 (0)	0 (0)	0 (0)	0 (0)
	white zone		0 (0)	0 (0)	0 (0)	0 (0)
kidney	brown		0 (0)	0 (0)	0 (0)	0 (0)
	black		0 (0)	0 (0)	0 (0)	0 (0)
testis	atrophic		0 (0)	0 (0)	1 (10)	0 (0)

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name NO. of Animals	2000 ppm 10 (%)	6000 ppm 10 (%)
subcutis	black		0 (0)	1 (10)
	jaundice		2 (20)	9 (90)
lung	black		0 (0)	1 (10)
spleen	enlarged		9 (90)	9 (90)
	black		10 (100)	9 (90)
	black patch/zone		0 (0)	0 (0)
	black zone		0 (0)	0 (0)
liver	brown		3 (30)	3 (30)
	black		5 (50)	7 (70)
	white zone		0 (0)	6 (60)
kidney	brown		1 (10)	3 (30)
	black		0 (0)	6 (60)
testis	atrophic		0 (0)	0 (0)

APPENDIX C 8-5

GROSS FINDINGS (THIRTEEN-WEEK STUDIES: SUMMARY)

MOUSE: FEMALE: SACRIFICED ANIMALS

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	74.1 ppm 10 (%)	222 ppm 10 (%)	667 ppm 10 (%)
subcutis	jaundice		0 (0)	0 (0)	0 (0)	0 (0)
lung	brown zone		0 (0)	0 (0)	0 (0)	0 (0)
spleen	enlarged		0 (0)	0 (0)	0 (0)	4 (40)
	black		0 (0)	0 (0)	2 (20)	8 (80)
	black patch/zone		0 (0)	1 (10)	0 (0)	0 (0)
heart	white zone		0 (0)	0 (0)	0 (0)	0 (0)
liver	enlarged		0 (0)	0 (0)	0 (0)	0 (0)
	brown		0 (0)	0 (0)	0 (0)	0 (0)
	black		0 (0)	0 (0)	0 (0)	0 (0)
kidney	brown		0 (0)	0 (0)	0 (0)	0 (0)
	black		0 (0)	0 (0)	0 (0)	1 (10)
ovary	cyst		1 (10)	0 (0)	0 (0)	0 (0)

Organ	Findings	Group Name NO. of Animals	2000 ppm 10 (%)	6000 ppm 9 (%)
subcutis	jaundice		2 (20)	9 (100)
lung	brown zone		0 (0)	1 (11)
spleen	enlarged		8 (80)	9 (100)
	black		8 (80)	9 (100)
	black patch/zone		0 (0)	0 (0)
heart	white zone		0 (0)	1 (11)
liver	enlarged		1 (10)	0 (0)
	brown		4 (40)	3 (33)
	black		4 (40)	4 (44)
kidney	brown		1 (10)	1 (11)
	black		0 (0)	6 (67)
ovary	cyst		0 (0)	0 (0)

APPENDIX C 9-1

ORGAN WEIGHT (THIRTEEN-WEEK STUDIES: SUMMARY), ABSOLUTE

RAT: MALE

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	Body weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	304± 15	0.268± 0.020	0.051± 0.005	2.853± 0.072	0.864± 0.095	1.007± 0.036
24.7 ppm	10	323± 14**	0.269± 0.036	0.053± 0.004	2.938± 0.064	0.943± 0.081*	1.023± 0.068
74.1 ppm	10	315± 6	0.255± 0.026	0.051± 0.004	2.913± 0.078	0.914± 0.048	1.014± 0.044
222 ppm	10	324± 12**	0.259± 0.037	0.054± 0.007	2.877± 0.143	0.946± 0.057*	1.061± 0.054
667 ppm	10	317± 14	0.303± 0.030	0.055± 0.003	2.856± 0.071	0.963± 0.041**	1.050± 0.040
2000 ppm	10	291± 13	0.218± 0.033**	0.057± 0.007	1.069± 0.150*	1.032± 0.067**	1.060± 0.054

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

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.848± 0.088	0.548± 0.025	7.407± 0.508	1.900± 0.041
24.7 ppm	10	1.949± 0.095*	0.590± 0.027	8.084± 0.494**	1.929± 0.044
74.1 ppm	10	1.945± 0.040*	0.671± 0.042	8.169± 0.355**	1.955± 0.128
222 ppm	10	1.953± 0.075*	1.121± 0.122**	8.623± 0.531**	1.934± 0.041
667 ppm	10	2.022± 0.052**	3.000± 0.306**	9.203± 0.387**	1.969± 0.100
2000 ppm	10	2.196± 0.096**	5.412± 0.324**	9.765± 0.360**	1.981± 0.047**

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

APPENDIX C 9-2

ORGAN WEIGHT (THIRTEEN-WEEK STUDIES: SUMMARY), ABSOLUTE

RAT: FEMALE

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	Body weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	174± 17	0.204± 0.037	0.059± 0.010	0.118± 0.027	0.580± 0.041	0.726± 0.062
24.7 ppm	10	179± 10	0.206± 0.016	0.058± 0.005	0.127± 0.013	0.605± 0.033	0.736± 0.049
74.1 ppm	10	179± 7	0.210± 0.028	0.058± 0.005	0.134± 0.044	0.608± 0.027	0.739± 0.048
222 ppm	10	177± 10	0.235± 0.032	0.058± 0.009	0.123± 0.019	0.622± 0.049	0.749± 0.033
667 ppm	10	176± 7	0.280± 0.068**	0.059± 0.006	0.130± 0.018	0.681± 0.059**	0.776± 0.044
2000 ppm	10	163± 9*	0.187± 0.022	0.060± 0.007	0.115± 0.018	0.695± 0.053**	0.770± 0.054

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

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.173± 0.119	0.369± 0.021	4.177± 0.596	1.726± 0.038
24.7 ppm	10	1.170± 0.074	0.396± 0.024	4.218± 0.211	1.746± 0.040
74.1 ppm	10	1.205± 0.051	0.482± 0.031	4.368± 0.303	1.764± 0.034
222 ppm	10	1.238± 0.058	0.955± 0.070**	4.697± 0.287	1.771± 0.033*
667 ppm	10	1.339± 0.066**	2.329± 0.233**	5.353± 0.507**	1.805± 0.029**
2000 ppm	10	1.376± 0.065**	4.102± 0.399**	5.730± 0.307**	1.825± 0.026**

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

APPENDIX C 9-3

ORGAN WEIGHT (THIRTEEN-WEEK STUDIES : SUMMARY), ABSOLUTE

MOUSE : MALE

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	Body weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	30.5± 2.4	0.046± 0.005	0.010± 0.002	0.236± 0.014	0.135± 0.009	0.140± 0.007
74.1 ppm	09	31.1± 1.9	0.042± 0.005	0.009± 0.002	0.233± 0.028	0.137± 0.010	0.142± 0.008
222 ppm	10	31.9± 2.4	0.046± 0.011	0.010± 0.002	0.218± 0.048	0.140± 0.009	0.146± 0.009
667 ppm	10	32.1± 3.0	0.045± 0.011	0.010± 0.002	0.243± 0.047	0.139± 0.008	0.138± 0.010
2000 ppm	10	29.1± 1.9	0.038± 0.004*	0.011± 0.003	0.238± 0.013	0.143± 0.010	0.145± 0.008
6000 ppm	10	23.9± 2.1**	0.034± 0.006**	0.013± 0.003*	0.171± 0.020**	0.154± 0.010**	0.157± 0.013**

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

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.396± 0.029	0.046± 0.006	1.040± 0.073	0.438± 0.018
74.1 ppm	09	0.394± 0.018	0.051± 0.009	1.062± 0.073	0.439± 0.014
222 ppm	10	0.397± 0.011	0.050± 0.005	1.094± 0.097	0.443± 0.014
667 ppm	10	0.410± 0.025	0.062± 0.012	1.133± 0.089	0.440± 0.010
2000 ppm	10	0.415± 0.034	0.169± 0.023**	1.199± 0.077**	0.448± 0.014
6000 ppm	10	0.414± 0.042	0.520± 0.053**	1.532± 0.113**	0.454± 0.024

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

APPENDIX C 9-4

ORGAN WEIGHT (THIRTEEN-WEEK STUDIES : SUMMARY), ABSOLUTE

MOUSE : FEMALE

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	Body weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	21.7± 1.6	0.048± 0.004	0.015± 0.003	0.041± 0.007	0.117± 0.010	0.144± 0.007
74.1 ppm	10	22.8± 1.6	0.049± 0.006	0.014± 0.003	0.041± 0.010	0.118± 0.011	0.149± 0.020
222 ppm	10	23.3± 2.8	0.052± 0.007	0.015± 0.002	0.042± 0.008	0.118± 0.008	0.144± 0.013
667 ppm	10	23.0± 1.3	0.045± 0.007	0.016± 0.003	0.043± 0.011	0.119± 0.007	0.147± 0.009
2000 ppm	10	22.3± 1.2	0.047± 0.005	0.015± 0.003	0.036± 0.005	0.131± 0.005**	0.149± 0.008
6000 ppm	09	19.9± 0.6	0.046± 0.007	0.014± 0.003	0.032± 0.006	0.138± 0.020**	0.162± 0.053

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

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.288± 0.010	0.059± 0.007	0.870± 0.057	0.455± 0.013
74.1 ppm	10	0.289± 0.024	0.062± 0.007	0.872± 0.043	0.446± 0.015
222 ppm	10	0.300± 0.018	0.063± 0.007	0.924± 0.067	0.459± 0.009
667 ppm	10	0.295± 0.016	0.111± 0.023**	0.957± 0.080*	0.459± 0.012
2000 ppm	10	0.304± 0.014	0.269± 0.032**	1.073± 0.083**	0.458± 0.010
6000 ppm	09	0.291± 0.017	0.508± 0.078**	1.293± 0.078**	0.441± 0.012

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

APPENDIX C 10-1

ORGAN WEIGHT (THIRTEEN-WEEK STUDIES : SUMMARY), RELATIVE

RAT : MALE

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	Body weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	304± 15	0.088± 0.006	0.017± 0.001	0.941± 0.047	0.285± 0.031	0.332± 0.011
24.7 ppm	10	323± 14**	0.083± 0.010	0.016± 0.002	0.910± 0.038	0.292± 0.019	0.317± 0.015
74.1 ppm	10	315± 6	0.081± 0.008	0.016± 0.001	0.926± 0.025	0.291± 0.013	0.323± 0.013
222 ppm	10	324± 12**	0.080± 0.010	0.017± 0.002	0.887± 0.032*	0.292± 0.010	0.327± 0.016
667 ppm	10	317± 14	0.095± 0.007	0.017± 0.001	0.903± 0.050	0.304± 0.012	0.332± 0.014
2000 ppm	10	291± 13	0.074± 0.009**	0.019± 0.002**	0.367± 0.052**	0.354± 0.016**	0.364± 0.011**

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

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.609± 0.021	0.181± 0.011	2.437± 0.077	0.627± 0.027
24.7 ppm	10	0.604± 0.032	0.183± 0.007	2.501± 0.102	0.598± 0.024
74.1 ppm	10	0.618± 0.010	0.213± 0.011	2.596± 0.093**	0.621± 0.039
222 ppm	10	0.602± 0.018	0.345± 0.030**	2.657± 0.086**	0.597± 0.026
667 ppm	10	0.639± 0.030	0.947± 0.098**	2.904± 0.041**	0.622± 0.031
2000 ppm	10	0.754± 0.018**	1.859± 0.099**	3.355± 0.063**	0.681± 0.028**

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

APPENDIX C 10-2

ORGAN WEIGHT (THIRTEEN-WEEK STUDIES: SUMMARY), RELATIVE

RAT: FEMALE

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	Body weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	174± 17	0.117± 0.017	0.034± 0.005	0.068± 0.018	0.334± 0.023	0.418± 0.036
24.7 ppm	10	179± 10	0.115± 0.005	0.032± 0.003	0.071± 0.007	0.339± 0.017	0.413± 0.030
74.1 ppm	10	179± 7	0.117± 0.015	0.032± 0.003	0.075± 0.025	0.339± 0.014	0.412± 0.028
222 ppm	10	177± 10	0.132± 0.012	0.033± 0.004	0.070± 0.009	0.352± 0.017	0.424± 0.020
667 ppm	10	176± 7	0.159± 0.036*	0.033± 0.003	0.074± 0.009	0.387± 0.024**	0.441± 0.021
2000 ppm	10	163± 9*	0.114± 0.008	0.037± 0.004	0.071± 0.009	0.426± 0.019**	0.472± 0.023**

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

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.674± 0.048	0.213± 0.018	2.392± 0.192	0.998± 0.095
24.7 ppm	10	0.656± 0.036	0.222± 0.011	2.365± 0.069	0.980± 0.048
74.1 ppm	10	0.672± 0.025	0.269± 0.012	2.434± 0.111	0.985± 0.043
222 ppm	10	0.701± 0.030	0.541± 0.041**	2.658± 0.089*	1.004± 0.048
667 ppm	10	0.762± 0.030**	1.323± 0.101**	3.040± 0.185**	1.028± 0.045
2000 ppm	10	0.844± 0.021**	2.512± 0.162**	3.514± 0.072**	1.122± 0.065**

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

APPENDIX C 10-3

ORGAN WEIGHT (THIRTEEN-WEEK STUDIES: SUMMARY), RELATIVE

MOUSE: MALE

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	Body weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	30.5± 2.4	0.152± 0.012	0.032± 0.006	0.776± 0.064	0.443± 0.035	0.462± 0.041
74.1 ppm	09	31.1± 1.9	0.135± 0.017	0.030± 0.007	0.752± 0.108	0.440± 0.024	0.457± 0.024
222 ppm	10	31.9± 2.4	0.144± 0.026	0.032± 0.006	0.695± 0.182	0.439± 0.033	0.457± 0.031
667 ppm	10	32.1± 3.0	0.140± 0.025	0.032± 0.007	0.757± 0.117	0.437± 0.043	0.434± 0.048
2000 ppm	10	29.1± 1.9	0.130± 0.019	0.039± 0.011	0.821± 0.088	0.492± 0.033*	0.501± 0.029
6000 ppm	10	23.9± 2.1**	0.141± 0.024	0.054± 0.011**	0.717± 0.087	0.647± 0.039**	0.661± 0.062**

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

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.300± 0.081	0.152± 0.021	3.414± 0.167	1.442± 0.129
74.1 ppm	09	1.269± 0.077	0.164± 0.027	3.410± 0.106	1.414± 0.072
222 ppm	10	1.248± 0.085	0.158± 0.015	3.426± 0.175	1.395± 0.105
667 ppm	10	1.283± 0.100	0.197± 0.053	3.538± 0.184	1.381± 0.133
2000 ppm	10	1.430± 0.120*	0.584± 0.083**	4.124± 0.180**	1.545± 0.105
6000 ppm	10	1.732± 0.092**	2.180± 0.187**	6.428± 0.326**	1.909± 0.134**

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

APPENDIX C 10-4

ORGAN WEIGHT (THIRTEEN-WEEK STUDIES : SUMMARY), RELATIVE

MOUSE : FEMALE

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	Body weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	21.7± 1.6	0.219± 0.018	0.071± 0.016	0.189± 0.039	0.541± 0.048	0.666± 0.042
74.1 ppm	10	22.8± 1.6	0.216± 0.024	0.063± 0.013	0.181± 0.046	0.520± 0.056	0.658± 0.098
222 ppm	10	23.3± 2.8	0.223± 0.029	0.065± 0.012	0.180± 0.033	0.512± 0.037	0.624± 0.060
667 ppm	10	23.0± 1.3	0.197± 0.029	0.069± 0.014	0.188± 0.048	0.521± 0.026	0.641± 0.052
2000 ppm	10	22.3± 1.2	0.211± 0.021	0.068± 0.011	0.159± 0.019	0.589± 0.029	0.669± 0.022
6000 ppm	09	19.9± 0.6	0.230± 0.035	0.072± 0.013	0.160± 0.030	0.691± 0.086**	0.807± 0.239

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

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.330± 0.091	0.269± 0.020	4.009± 0.183	2.105± 0.198
74.1 ppm	10	1.276± 0.150	0.274± 0.034	3.838± 0.231	1.969± 0.182
222 ppm	10	1.296± 0.100	0.274± 0.030	3.995± 0.315	1.994± 0.221
667 ppm	10	1.289± 0.073	0.482± 0.083*	4.167± 0.232	2.005± 0.120
2000 ppm	10	1.363± 0.062	1.205± 0.125**	4.805± 0.136**	2.055± 0.088
6000 ppm	09	1.461± 0.095*	2.546± 0.333**	6.481± 0.229**	2.214± 0.094

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

APPENDIX C 11-1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDIES : SUMMARY)

RAT : MALE : SACRIFICED ANIMALS

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name	Control				24.7 ppm				74.1 ppm				222 ppm			
		No. of Animals	10				10				10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Respiratory system]																		
nasal cavit	inflammation		1 (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)	0 (0)	0 (0)
[Hematopoietic system]																		
bone marrow	erythropoiesis:increased		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 (60)	0 (0)	0 (0)	0 * (0)
spleen	congestion		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 ** (0)	3 (30)	7 (70)	0 (0)	0 ** (0)
	deposit of hemosiderin		0 (0)	10 (100)	0 (0)	0 (0)	1 (10)	9 (90)	0 (0)	0 (0)	0 (0)	2 (20)	8 (80)	0 ** (0)	0 (0)	0 (0)	10 (100)	0 ** (0)
	extramedullary hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 ** (0)	5 (50)	5 (50)	0 (0)	0 ** (0)
	capsule 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)	7 (70)	0 (0)	0 (0)	0 ** (0)
[Circulatory system]																		
heart	granulation		2 (20)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Digestive system]																		
liver	herniation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	8 (80)	0 (0)	0 (0)	0 ** (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name / No. of Animals	667 ppm 10 <1> (%)	<2> (%)	<3> (%)	<4> (%)	2000 ppm 10 <1> (%)	<2> (%)	<3> (%)	<4> (%)
[Respiratory system]										
nasal cavit	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]										
bone marrow	erythropoiesis:increased		0 (0)	10 (100)	0 (0)	0 ** (0)	1 (10)	0 (0)	9 (90)	0 ** (0)
spleen	congestion		1 (10)	1 (10)	8 (80)	0 ** (0)	0 (0)	1 (10)	9 (90)	0 ** (0)
	deposit of hemosiderin		1 (10)	0 (0)	9 (90)	0 ** (0)	0 (0)	0 (0)	10 (100)	0 ** (0)
	extramedullary hematopoiesis		0 (0)	10 (100)	0 (0)	0 ** (0)	0 (0)	10 (100)	0 (0)	0 ** (0)
	capsule hyperplasia		0 (0)	10 (100)	0 (0)	0 ** (0)	9 (90)	0 (0)	0 (0)	0 ** (0)
[Circulatory system]										
heart	granulation		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
[Digestive system]										
liver	herniation		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		10 (100)	0 (0)	0 (0)	0 ** (0)	0 (0)	10 (100)	0 (0)	0 ** (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

Organ	Findings	Group Name	Control				24.7 ppm				74.1 ppm				222 ppm			
		No. of Animals	10				10				10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Digestive system]																		
liver	granulation		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
	swelling:central		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Urinary system]																		
kidney	basophilic change		3 (30)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (40)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	4 (40)	0 (0)	0 (0)	0 (0)
	eosinophilic body		4 (40)	6 (60)	0 (0)	0 (0)	2 (20)	7 (70)	0 (0)	0 (0)	0 (0)	8 (80)	1 (10)	0 (0)	0 (0)	8 (80)	2 (20)	0 * (0)
[Reproductive system]																		
testis	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	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		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Special sense organs/appandage]																		
Harder gl	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

Organ	Findings	Group Name	667 ppm				2000 ppm			
		No. of Animals	10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Digestive system]										
liver	granulation		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		4 (40)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 ** (0)
	swelling:central		0 (0)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 ** (0)
[Urinary system]										
kidney	basophilic change		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		8 (80)	0 (0)	2 (20)	0 ** (0)	0 (0)	10 (100)	0 (0)	0 ** (0)
	eosinophilic body		0 (0)	0 (0)	10 (100)	0 ** (0)	1 (10)	0 (0)	9 (90)	0 ** (0)
[Reproductive system]										
testis	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	9 (90)	1 (10)	0 ** (0)
	interstitial cell hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	7 (70)	0 (0)	0 (0)	0 ** (0)
[Special sense organs/appandage]										
Harder gl	inflammation		1 (10)	8 (80)	1 (10)	0 ** (0)	4 (40)	2 (20)	0 (0)	0 * (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

APPENDIX C 11-2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDIES : SUMMARY)

RAT : FEMALE : SACRIFICED ANIMALS

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name	Control				24.7 ppm				74.1 ppm				222 ppm			
		No. of Animals	10				10				10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Hematopoietic system]																		
bone marrow	granulation		1 (10)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	4 (40)	1 (10)	0 (0)	0 (0)
	erythropoiesis:increased		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 ** (0)
spleen	congestion		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 ** (0)	1 (10)	9 (90)	0 (0)	0 ** (0)
	deposit of hemosiderin		0 (0)	10 (100)	0 (0)	0 (0)	0 (0)	9 (90)	1 (10)	0 (0)	0 (0)	0 (0)	10 (100)	0 ** (0)	0 (0)	0 (0)	10 (100)	0 ** (0)
	extramedullary hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	6 (60)	0 (0)	0 (0)	0 * (0)	1 (10)	9 (90)	0 (0)	0 ** (0)
	capsule 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)	10 (100)	0 (0)	0 (0)	0 ** (0)
[Digestive system]																		
liver	herniation		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		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 (40)	0 (0)	0 (0)	0 (0)
	granulation		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	1 (10)	0 (0)
	extramedullary hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Urinary system]																		
kidney	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 ** (0)	10 (100)	0 (0)	0 (0)	0 ** (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name	667 ppm				2000 ppm			
		No. of Animals	10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Hematopoietic system]										
bone marrow	granulation		3 (30)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	erythropoiesis:increased		0 (0)	1 (10)	9 (90)	0 ** (0)	0 (0)	0 (0)	10 (100)	0 ** (0)
spleen	congestion		0 (0)	6 (60)	4 (40)	0 ** (0)	0 (0)	0 (0)	10 (100)	0 ** (0)
	deposit of hemosiderin		0 (0)	0 (0)	10 (100)	0 ** (0)	0 (0)	0 (0)	10 (100)	0 ** (0)
	extramedullary hematopoiesis		0 (0)	10 (100)	0 (0)	0 ** (0)	0 (0)	4 (40)	6 (60)	0 ** (0)
	capsule hyperplasia		1 (10)	8 (80)	0 (0)	0 ** (0)	4 (40)	0 (0)	0 (0)	0 (0)
[Digestive system]										
liver	herniation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		10 (100)	0 (0)	0 (0)	0 ** (0)	0 (0)	10 (100)	0 (0)	0 ** (0)
	granulation		3 (30)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		1 (10)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 ** (0)
[Urinary system]										
kidney	deposit of hemosiderin		0 (0)	9 (90)	1 (10)	0 ** (0)	1 (10)	0 (0)	9 (90)	0 ** (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0057
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name	Control				24.7 ppm				74.1 ppm				222 ppm			
		No. of Animals	10				10				10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Urinary system]																		
kidney	mineralization		9 (90)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)	7 (70)	1 (10)	0 (0)	0 (0)
[Reproductive system]																		
uterus	dilatation		2 (20)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Special sense organs/appandage]																		
Harder gl	inflammation		2 (20)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	4 (40)	2 (20)	0 (0)	0 (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

Organ	Findings	Group Name	667 ppm				2000 ppm			
		No. of Animals	10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Urinary system]										
kidney	mineralization		7 (70)	0 (0)	0 (0)	0 (0)	5 (50)	0 (0)	0 (0)	0 (0)
[Reproductive system]										
uterus	dilatation		2 (20)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
[Special sense organs/appandage]										
Harder gl	inflammation		0 (0)	9 (90)	1 (10)	0 (0) **	1 (10)	7 (70)	2 (20)	0 (0) **

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

APPENDIX C 11-3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDIES : SUMMARY)

MOUSE : FEMALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 13W)

Organ	Findings	Group Name / No. of Animals	Control 0 <1> (%)	<2> (%)	<3> (%)	<4> (%)	74.1 ppm 0 <1> (%)	<2> (%)	<3> (%)	<4> (%)	222 ppm 0 <1> (%)	<2> (%)	<3> (%)	<4> (%)	667 ppm 0 <1> (%)	<2> (%)	<3> (%)	<4> (%)
[Hematopoietic system]																		
bone marrow	deposit of hemosiderin		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	erythropoiesis:increased		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
spleen	deposit of hemosiderin		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
[Circulatory system]																		
heart	dilatation		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
[Digestive system]																		
liver	deposit of hemosiderin		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	extramedullary hematopoiesis		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
[Urinary system]																		
kidney	vacuolization of proximal tubule		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)

<1>:Slight <2>:Moderate <3>:Marked <4>:Severe

Organ	Findings	Group Name	2000 ppm				6000 ppm			
		No. of Animals	0				1			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Hematopoietic system]										
bone marrow	deposit of hemosiderin		- (-)	- (-)	- (-)	- (-)	0 (0)	1 (100)	0 (0)	0 (0)
	erythropoiesis:increased		- (-)	- (-)	- (-)	- (-)	1 (100)	0 (0)	0 (0)	0 (0)
spleen	deposit of hemosiderin		- (-)	- (-)	- (-)	- (-)	0 (0)	0 (0)	1 (100)	0 (0)
[Circulatory system]										
heart	dilatation		- (-)	- (-)	- (-)	- (-)	1 (100)	0 (0)	0 (0)	0 (0)
[Digestive system]										
liver	deposit of hemosiderin		- (-)	- (-)	- (-)	- (-)	1 (100)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		- (-)	- (-)	- (-)	- (-)	1 (100)	0 (0)	0 (0)	0 (0)
[Urinary system]										
kidney	vacuolization of proximal tubule		- (-)	- (-)	- (-)	- (-)	0 (0)	0 (0)	1 (100)	0 (0)

<1>:Slight <2>:Moderate <3>:Marked <4>:Severe

APPENDIX C 11-4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDIES : SUMMARY)

MOUSE : MALE : SACRIFICED ANIMALS

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name	Control				74.1 ppm				222 ppm				667 ppm			
		No. of Animals	10				9				10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Hematopoietic system]																		
bone marrow	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	erythropoiesis:increased		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
spleen	congestion		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		2 (20)	0 (0)	0 (0)	0 (0)	3 (33)	0 (0)	0 (0)	0 (0)	9 (90)	0 (0)	0 (0)	0 (0) **	4 (40)	6 (60)	0 (0)	0 (0) **
	deposit of melanin		1 (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)	0 (0)	0 (0)
	extramedullary hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	8 (80)	1 (10)	0 (0)	0 (0) **
[Circulatory system]																		
heart	thrombus		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Digestive system]																		
salivary gl	lymphocytic infiltration		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
liver	thrombus		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	necrosis:focal		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

Organ	Findings	Group Name	2000 ppm				6000 ppm			
		No. of Animals	10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Hematopoietic system]										
bone marrow	deposit of hemosiderin		10 (100)	0 (0)	0 (0)	0 ** (0)	2 (20)	8 (80)	0 (0)	0 ** (0)
	erythropoiesis:increased		7 (70)	0 (0)	0 (0)	0 ** (0)	8 (80)	0 (0)	0 (0)	0 ** (0)
spleen	congestion		4 (40)	6 (60)	0 (0)	0 ** (0)	1 (10)	7 (70)	1 (10)	0 ** (0)
	deposit of hemosiderin		0 (0)	1 (10)	9 (90)	0 ** (0)	0 (0)	0 (0)	9 (90)	0 ** (0)
	deposit of melanin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		0 (0)	10 (100)	0 (0)	0 ** (0)	0 (0)	1 (10)	8 (80)	0 ** (0)
[Circulatory system]										
heart	thrombus		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
[Digestive system]										
salivary gl	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
liver	thrombus		0 (0)	0 (0)	0 (0)	0 (0)	7 (70)	1 (10)	0 (0)	0 ** (0)
	necrosis:focal		0 (0)	0 (0)	0 (0)	0 (0)	8 (80)	0 (0)	0 (0)	0 ** (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

Organ	Findings	Group Name	Control				74.1 ppm				222 ppm				667 ppm			
		No. of Animals	10				9				10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Digestive system]																		
liver	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	swelling:central		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
gall bladd	inflammation		1 (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)	0 (0)	0 (0)
[Urinary system]																		
kidney	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 (10)	0 (0)	0 (0)	0 (0)
	basophilic change		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	vacuolization of proximal tubule		9 (90)	0 (0)	0 (0)	0 (0)	8 (89)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)
	mineralization:papilla		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Endocrine system]																		
adrenal	accesory cortical nodule		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

Organ	Findings	Group Name	2000 ppm				6000 ppm			
		No. of Animals	10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Digestive system]										
liver	deposit of hemosiderin		9 (90)	0 (0)	0 (0)	0 ** (0)	0 (0)	10 (100)	0 (0)	0 ** (0)
	extramedullary hematopoiesis		3 (30)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 ** (0)
	swelling:central		1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	9 (90)	0 (0)	0 ** (0)
gall bladd	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Urinary system]										
kidney	cyst		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	basophilic change		1 (10)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		10 (100)	0 (0)	0 (0)	0 ** (0)	0 (0)	10 (100)	0 (0)	0 ** (0)
	vacuolization of proximal tubule		9 (90)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 ** (0)
	mineralization:papilla		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Endocrine system]										
adrenal	accesory cortical nodule		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name	Control				74.1 ppm				222 ppm				667 ppm			
		No. of Animals	10				9				10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Reproductive system]																		
testis	atrophy		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 (10)	0 (0)	0 (0)	0 (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

Organ	Findings	Group Name	2000 ppm				6000 ppm			
		No. of Animals	10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Reproductive system]										
testis	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0) **

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

APPENDIX C 11-5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDIES : SUMMARY)

MOUSE : FEMALE : SACRIFICED ANIMALS

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name / No. of Animals	Control 10				74.1 ppm 10				222 ppm 10				667 ppm 10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Respiratory system]																		
lung/bronch	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]																		
bone marrow	deposit of hemosiderin		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 (20)	0 (0)	0 (0)	0 (0)
	erythropoiesis:increased		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 (10)	0 (0)	0 (0)	0 (0)
lymph node	congestion		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
spleen	congestion		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	8 (80)	0 (0)	0 (0)	0 (0) **
	deposit of hemosiderin		9 (90)	0 (0)	0 (0)	0 (0)	9 (90)	0 (0)	0 (0)	0 (0)	4 (40)	6 (60)	0 (0)	0 (0) *	0 (0)	1 (10)	9 (90)	0 (0) **
	deposit of melanin		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		10 (100)	0 (0)	0 (0)	0 (0)	9 (90)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)	3 (30)	6 (60)	1 (10)	0 (0) **
[Circulatory system]																		
heart	thrombus		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Digestive system]																		
salivary gl	lymphocytic infiltration		1 (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)	0 (0)	0 (0)

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

Organ	Findings	Group Name	2000 ppm				6000 ppm			
		No. of Animals	10				9			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Respiratory system]										
lung/bronch	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)
[Hematopoietic system]										
bone marrow	deposit of hemosiderin		10 (100)	0 (0)	0 (0)	0 ** (0)	0 (0)	9 (100)	0 (0)	0 ** (0)
	erythropoiesis:increased		8 (80)	0 (0)	0 (0)	0 ** (0)	9 (100)	0 (0)	0 (0)	0 ** (0)
lymph node	congestion		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
spleen	congestion		0 (0)	10 (100)	0 (0)	0 ** (0)	0 (0)	9 (100)	0 (0)	0 ** (0)
	deposit of hemosiderin		0 (0)	0 (0)	10 (100)	0 ** (0)	0 (0)	0 (0)	9 (100)	0 ** (0)
	deposit of melanin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		0 (0)	10 (100)	0 (0)	0 ** (0)	0 (0)	0 (0)	9 (100)	0 ** (0)
[Circulatory system]										
heart	thrombus		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)
[Digestive system]										
salivary gl	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0058
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

Organ	Findings	Group Name / No. of Animals	Control 10				74.1 ppm 10				222 ppm 10				667 ppm 10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Digestive system]																		
liver	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)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	swelling:central		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Urinary system]																		
kidney	basophilic change		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 (10)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mineralization:papilla		1 (10)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
[Endocrine system]																		
thyroid	lymphocytic infiltration		1 (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)	0 (0)	0 (0)
adrenal	accesory cortical nodule		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Body cavities]																		
adipose	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)	0 (0)	0 (0)	0 (0)	0 (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

Organ	Findings	Group Name	2000 ppm				6000 ppm			
		No. of Animals	10				9			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Digestive system]										
liver	necrosis:focal		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		10 (100)	0 (0)	0 (0)	0 ** (0)	0 (0)	9 (100)	0 (0)	0 ** (0)
	extramedullary hematopoiesis		8 (80)	0 (0)	0 (0)	0 ** (0)	9 (100)	0 (0)	0 (0)	0 ** (0)
	swelling:central		9 (90)	0 (0)	0 (0)	0 ** (0)	1 (11)	8 (89)	0 (0)	0 ** (0)
[Urinary system]										
kidney	basophilic change		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		10 (100)	0 (0)	0 (0)	0 ** (0)	0 (0)	9 (100)	0 (0)	0 ** (0)
	mineralization:papilla		1 (10)	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)
[Endocrine system]										
thyroid	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
adrenal	accesory cortical nodule		0 (0)	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)
[Body cavities]										
adipose	granulation		0 (0)	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

APPENDIX C 12-1

IDENTITY AND PURITY OF p-CNB

PERFORMED AT THE JAPAN BIOASSAY LABORATORY

(THIRTEEN-WEEK STUDIES)

IDENTITY AND PURITY OF p-CNB PERFORMED AT THE JAPAN BIOASSAY LABORATORY
(THIRTEEN-WEEK STUDIES)

Lot no.CDM5913

A.Spectral data

Infrared

Instrument : Hitachi 270-30

Cell : KBr

Slit : Medium

Results : Wave Number
(CM^{-1})

470	470
540	540
620	
670	680
740	740
840	850
1020	1020
1090	1100
1120	1120
1170	1180
1280	1280
1310	1320
1350	1350
1420	1420
1470	1480
1520	1520
1580	1580
1600	1610
3100	3100

(Sadtler handbook
by Sadtler Researc
Laboratories,Inc.)

B.Gas Chromatography

Instrument	: Shimadzu GC-9A
Column	: THERM 1000,50m,0.25ϕ
Column Temperature	: 180°C
Flow Rate	: 1ml/min
Detector	: Flame Ionization Detecter(FID)
Injection Volume	: 1μl
Results	: Only one major peak

Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	Area (percent of Major peak)
1	4.703	1.00	100

C. Conclusions:The results of the infrared spectra agreed with the Literature values.Impurity was not detected in test substance by Gas chromatography.

APPENDIX C 12-2

STABILITY OF p-CNB AT THE JAPAN BIOASSAY LABORATORY

(THIRTEEN-WEEK STUDIES)

STABILITY OF p-CNB AT THE JAPAN BIOASSAY LABORATORY(THIRTEEN WEEK STUDIES)

Lot no.CDM5913

A.Sample storage: p-CNB were stored for about thirteen weeks at 5°C.

B.Spectral data

Infrared

Instrument : Hitachi 270-30

Cell : KBr

Slit : Medium

Results : Wave Number (CM^{-1})

Previous determined of test (08/28/84)	After determined of test (12/06/84)
470	470
540	540
680	680
740	740
850	850
1020	1020
1100	1100
1120	1120
1180	1180
1280	1280
1320	1320
1350	1350
1420	1420
1480	1480
1520	1520
1580	1580
1610	1610
3100	3100

C.Gas Chromatography

Instrument : Shimadzu GC-9A

Column : THERM 1000,50m,0.25 ϕ

Column Temperature : 180°C

Flow Rate : 1ml/min

Detector : Flame Ionization Detecter(FID)

Injection Volume : 1 μ l

Results : Only one major peak

Date	Retention Time(min)	Retention Time Relative to Major Peak	Area (percent of Major peak)
08/28/84	4.703	1.00	100
12/06/84	4.702	1.00	100

D. Conclusions:The results of the Infrared spectra agreed with the previous determine of test Values.Impurity was not detected in test substance by Gas chromatography.
Consequently,p-CNB was stable as the chemical when stored for about thirteen weeks at temperatures to 5°C.

APPENDIX C 12-3

RESULTS OF ANALYSYS OF FORMULATED DIETS

IN THE THIRTEEN-WEEK STUDIES OF p-CNB

RESULTS OF ANALYSIS OF FORMULATED DIETS IN THE THIRTEEN-WEEK STUDIES OF p-CNB

(Rat)

	Concentration of p-CNB in feed for Taget Concentration(ppm)				
Date Mixed	24.7(a)	74.1(a)	222 (a)	667 (a)	2000 (a)
11/20/84	20.9(84.5)	58.7(79.3)	200.8(90.5)	657.2(98.5)	2058.8(102.9)

(Mouse)

	Concentration of p-CNB in feed for Taget Concentration(ppm)				
Date Mixed	74.1(a)	222 (a)	667 (a)	2000 (a)	6000 (a)
11/20/84	58.7(79.3)	200.8(90.5)	657.2(98.5)	2058.8(102.9)	5185.8(86.4)

(a) Determined as a percent of taget

APPENDIX C 12-4

RESULTS OF SUTABILITY OF FORMULATED DIETS IN THE THIRTEEN-WEEK STUDIES OF p-CNB

RESULT OF STABILITY OF FORMULATED DIETS IN THE THIRTEEN-WEEK STUDIES OF p-CNB

(Rat)

	Concentration of p-CNB in feed for Taget Concentration(ppm)		
Date Mixed	24.7(a)	74.1(a)	2000 (a)
11/20/84(b)	20.9	58.7	2058.8
11/27/84	15.6(74.6)	45.4(77.3)	1571.3(76.3)

(Mouse)

	Concentration of p-CNB in feed for Taget Concentration(ppm)		
Date Mixed	74.1(a)	2000 (a)	6000
11/20/84(b)	58.7	2058.8	5185.8
11/27/84	45.4(77.3)	1571.3(76.3)	4466.5(86.1)

(a) Determined as a percent of taget

(b) Formulated