ブチル 2,3-エポキシプロピル エーテルのマウスを用いた吸入による 2 週間毒性試験報告書

試験番号:0412

APPENDICES

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APPENDIX A 1

CLINICAL OBSERVATION: SUMMARY, MOUSE: MALE

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

SEX : MALE

PAGE: 1

| Clinical sign | Group Name | Admini | stration We | eek-day | | | |
|-------------------------|------------|--------|-------------|---------|-----|------------|--|
| | - | 1-2 | 1-4 | 1-7 | 2-3 | 2-7 | |
| | | | | | | | |
| FROG BELLY | Control | 0 | 0 | 0 | 0 | 0 | |
| | 38ppm | 0 | 0 | 0 | 0 | 0 | |
| | 75ppm | 0 | 0 | 0 | 0 | 0 | |
| | 150ppm | 0 | 4 | 0 | 0 | 0 | |
| | 300ppm | 0 | 0 | 0 | 0 | 0 | |
| | 600ppm | 0 | 0 | - | - | - . | |
| RESPIRATORY SOUND ABNOR | Control | 0 | 0 | 0 | 0 | 0 | |
| | 38ppm | 0 | 0 | 0 | 0 | 0 | |
| | 75ppm | 0 | 0 | 0 | 0 | 0 | |
| | 150ppm | 0 | 0 | 0 | 0 | 0 | |
| | 300ppm | 0 | 3 | 0 | 0 | 0 | |
| | 600ppm | 2 | 0 | _ | _ | - | |

(HAN190)

APPENDIX A 2

CLINICAL OBSERVATION: SUMMARY, MOUSE: FEMALE

CLINICAL OBSERVATION (SUMMARY)

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1 2

ALL ANIMALS

| SEX : | FEMALE | | | | |
|-------|--------|--|--|--|--|
| | | | | | |

| Clinical sign | Group Name | Admini | stration We | ek-day | | |
|-------------------------|------------|--------|-------------|--------|-----|-----|
| - | - | 1-2 | 1-4 | 1-7 | 2-3 | 2-7 |
| | | | | | | |
| FROG BELLY | Control | 0 | 0 | 0 | 0 | 0 |
| FROG BELLI | Control | | | 0 | 0 | 0 |
| | 38ppm | 0 | 0 | 0 | 0 | 0 |
| | 75ppm | 0 | 0 | 0 | 0 | 0 |
| | 150ppm | 0 | 5 | 0 | 0 | 0 |
| | 300ppm | 0 | 0 | 0 | 0 | 0 |
| | 600ppm | 0 | 0 | - | - | - |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 |
| | 38ppm | 0 | 0 | 0 | 0 | 0 |
| | 75ppm | 0 | 0 | 0 | 0 | 0 |
| | 150ppm | 0 | 0 | 0 | 0 | 0 |
| | 300ppm | 0 | 0 | 1 | 0 | 0 |
| | 600ppm | 0 | 0 | | _ | _ |
| RESPIRATORY SOUND ABNOR | Control | 0 | 0 | 0 | 0 | 0 |
| | 38ppm | 0 | n | 0 | Ö | n |
| | 75ppm | n | ñ | 0 | 0 | 0 |
| | 150ppm | n | ň | 0 | Ö | Ŏ |
| | 300ppm | 0 | 0 | 0 | 0 | 0 |
| | | 3 | ٥ | - | - | - |
| | 600ppm | 3 | 0 | ~ | _ | _ |
| | | | | | | |

(HAN190)

BAIS 3

PAGE: 2

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, MOUSE : MALE (2-WEEK STUDY)

ANIMAL : MOUSE Crj:BDF1

UNIT : g

REPORT TYPE : A1 2

SEX : MALE

BODY WEIGHT CHANGES

(SUMMARY)

ALL ANIMALS

| Vame | Administration | week-day | | | | |
|----------------------|-----------------|--------------|-------------|-----------------|-------------|-------------|
| | 0-0 | 1-2 | 1-4 | 1-7 | 2-3 | 2-7 |
| Control | 23.1± 0.9 | 23.8± 1.1 | 23.8± 1.0 | 24.6± 1.2 | 24.8± 1.4 | 25.1± 1.4 |
| 38ppm | 23.0± 0.8 | 23.6± 1.1 | 23.2± 1.2 | 23.7± 1.0 | 24.1± 0.8 | 24.4± 0.7 |
| 75ppm | 23.0± 0.8 | 23.6± 0.9 | 22.9± 0.7 | 23.8± 0.8 | 23.9± 1.0 | 24. 2± 1. 2 |
| 150ppm | .23.0± 0.8 | 22.7± 0.5 | 22.0± 0.8* | 22.0± 0.6** | 22.0± 0.4** | 22.4± 0.5** |
| 300ppm | 23.0± 0.8 | 21.0± 0.9** | 18.1± 0.7** | 18.7± 0.7** | 18.6± 0.6** | 19.5± 0.8** |
| 600ppm | 23.0± 0.9 | 20.6± 1.1** | - | - | - | - |
| | | | | | | |
| gnificant difference | ce; *: P ≤ 0.05 | **: P ≤ 0.01 | | Test of Dunnett | | |

(HAN260)

BAIS 3

PAGE: 1

APPENDIX B 2

BODY WEIGHT CHANGES: SUMMARY, MOUSE: FEMALE

ANIMAL : MOUSE Crj:BDF1

UNIT : g

REPORT TYPE : A1 2

BODY WEIGHT CHANGES ALL ANIMALS (SUMMARY)

(000)

SEX: FEMALE

| lame | Administration | week-day | | | | | |
|---------------------|----------------|---------------|--------------|-----------------|-------------|--------------|--|
| | 0-0 | 1-2 | 1-4 | 1-7 | 2-3 | 2-7 | |
| Control | 19.1± 0.6 | 19.5± 0.4 | 19.8± 0.5 | 20.3± 0.5 | 20.7± 0.3 | 21.0± 0.9 | |
| 38ppm | 19.0± 0.7 | 19.2± 0.4 | 19.4± 0.9 | 20.2± 1.0 | 20.1± 1.0 | 20.4± 0.8 | |
| 75ppm | 19.0± 0.7 | 18.9± 0.7 | 19.0± 0.7 | 19.5± 0.7 | 19.1± 0.5** | 20.2± 0.7 | |
| 150ppm | 19.0± 0.7 | 18.5± 0.6 | 18.3± 0.8* | 18.2± 0.6** | 18.1± 0.5** | 18.5± 1.3** | |
| 300ppm | 19.1± 0.7 | 17.5± 0.3** | 15.4± 0.9** | 14.9± 1.0** | 15.1± 1.1** | 15.8± 0.8** | |
| 600ppm | 19.0± 0.7 | 16.6± 1.1** | - | - | - | - | |
| | | | | | | | |
| gnificant differenc | ce; *:P≦0.05 | ** : P ≤ 0.01 | | Test of Dunnett | | | |

(HAN260)

BAIS 3

PAGE: 2

APPENDIX C 1

FOOD CONSUMPTION CHANGES: SUMMARY, MOUSE: MALE

ANIMAL : MOUSE Crj:BDF1

UNIT : g
REPORT TYPE : A1 2

FOOD CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

| oup Name | Administration 1-7(6) | week-day(effective) 2-7(7) | | |
|-----------------------|--------------------------|-------------------------------|-----------------|--|
| Control | 4.2± 0.3 | 4.0± 0.2 | | |
| 38ppm | 4.0± 0.3 | 4.0± 0.1 | | |
| 75ppm | 4.0± 0.4 | 3.8± 0.4 | | |
| 150ppm | 3.4± 0.2** | 3.4± 0.2** | | |
| 300ppm | 2.4± 0.2** | 3.5± 0.2* | | |
| 600ppm | - | - | | |
| | | | | |
| Significant differend | ce; *: P ≤ 0.05 | ** : P ≦ 0.01 | Test of Dunnett | |

(HAN260)

APPENDIX C 2

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : FEMALE (2-WEEK STUDY)

ANIMAL : MOUSE Crj:BDF1
UNIT : g

REPORT TYPE : A1 2

FOOD CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

| p Name | Administration | week-day(effective) | | |
|------------------------|-----------------|---------------------|-----------------|------|
| | 1-7 (6) | 2-7 (7) | | |
| Control | 3.9± 0.2 | 3.6± 0.3 | | |
| 38ppm | 3.6± 0.3 | 3.5± 0.1 | | |
| 75ppm | 3.5± 0.3 | 3.4± 0.2 | | |
| 150ppm | 2.9± 0.1** | 3.0± 0.1* | | |
| 300ppm | 1.8± 0.3** | 2.9± 0.1** | | |
| 600ppm | - | - | | |
| | | | | |
| Significant difference | ce; *: P ≤ 0.05 | ** : P ≦ 0.01 | Test of Dunnett | |

(HAN260)

APPENDIX D 1

HEMATOLOGY: SUMMARY, MOUSE: MALE

STUDY NO. : 0412 ANIMAL : MOUSE Crj:BDF1

HEMATOLOGY (SUMMARY) ALL ANIMALS (3W)

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

PAGE: 1

| roup Name | NO. of Animals | RED BLO | OOD CELL | HEMOGLO g/dl | BIN | HEMATOC % | RIT | MCV f & | | MCH PE | | MCHC g/dl | | PLATELE 1 0³/µ | |
|-----------|-------------------|---------|----------|-----------------|------|--------------|------|------------|------|-----------|------|--------------|-----|-------------------|-----|
| Control | 5 | 11.40± | 0. 23 | 17.0± | 0.5 | 55.3± | 1. 2 | 48.5± | 0.4 | 14.9± | 0. 2 | 30.7± | 0.4 | 1295± | 90 |
| 38ppm | 5 | 11.33± | 0. 32 | 17.0± | 0.4 | 55.0± | 1.8 | 48.6± | 0.6 | 15.0± | 0.1 | 30.9± | 0.5 | 1294± | 71 |
| 75ppm | 4 | 11.28± | 0.48 | 17.0± | 0.6 | 54.9± | 2. 3 | 48.7± | 1.1 | 15.0± | 0. 2 | 30.9± | 0.7 | 1240± | 121 |
| 150ppm | 5 | 11.26± | 0.21 | 16.9± | 0.3 | 54, 4± | 1. 5 | 48.3± | 0.5 | 15.0± | 0.0 | 31.0± | 0.3 | 1223生 | 48 |
| 300ppm | 4 | 10.99± | 0. 23 | 16.3± | 0, 3 | 52.1± | 1.3 | 47.4± | 0, 5 | 14.8生 | 0.1 | 31.3± | 0.2 | 1209± | 166 |
| 600ppm | 0 | - | | - | | - | | - | | - | | - | | - | |

(HCL070)

ANIMAL : MOUSE Crj:BDF1

HEMATOLOGY (SUMMARY) ALL ANIMALS (3W)

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

PAGE: 2

| roup Name | NO. of Animals | WBC 1 O³∕µl | Dif N-BAND | ferential | N-SEG | <u></u> | EOSINO | | BASO | | MONO | | LYMPHO | | OTHER | |
|-------------|-------------------|----------------|---------------|-----------|-------|---------|--------|---------|------|---|------|---|--------|-------------|-------|---|
| Control | 5 | 1.70± 0.90 | 1± | 1 | 12± | 4 | 1± | 1 | 0± | 0 | 1± | 1 | 85± | 3 | 0± | C |
| 38ppm | 5 | 1.65± 0.68 | 1± | 1 | 12± | 5 | 1± | 1 | 0± | 0 | 2± | 1 | 84± | 5 | 0± | (|
| 75ppm | 4 | 1.67± 0.71 | 1± | 1 | 9± | 2 | 1± | 1 | 0± | 0 | 2± | 1 | 88± | 3 | 0± | (|
| 150ppm | 5 | 1.08± 0.64 | 0± | 0 | 10± | 2 | 1± | 1 | 0± | 0 | 3± | 2 | 86± | 4 | 0± | |
| 300ppm | 4 | 0.80± 0.30 | 1± | 1 | 30± | 17 | 1± | 1 | 0± | 0 | 2± | 2 | 67± | 17 | 0± | |
| 600ppm | 0 | - | - | | - | | - | | - | | | | - | | _ | |
| Significant | difference | * : P ≤ 0.05 | **: P ≦ | 0.01 | | | Test | of Dunn | ıett | | - | | | | | |

APPENDIX D 2

HEMATOLOGY: SUMMARY, MOUSE: FEMALE

HEMATOLOGY (SUMMARY)

ANIMAL : MOUSE Crj:BDF1

ALL ANIMALS (3W)

MEASURE. TIME: 1 SEX: FEMALE

REPORT TYPE : A1

PAGE: 3

| oup Name | NO. of Animals | RED BLC 1 O ^s /p | OOD CELL | HEMOGLO g/dl | BIN | HEMATOC % | RIT | MCV f l | | MCH pg | | MCHC g/dl | | PLATELET 1 Ο³ / μί | |
|----------|-------------------|--------------------------------|----------|-----------------|-------|--------------|-------|------------|------|-----------|------|--------------|------|-----------------------|----|
| Control | 4 | 11.34± | 0. 22 | 17.0± | 0.5 | 54.1± | 1.0 | 47.7± | 0.1 | 15.0± | 0.1 | 31.5± | 0.3 | 1099± | 64 |
| 38ppm | 4 | 11.28± | 0.40 | 17.0± | 0.5 | 54.4± | 2. 4 | 48.3± | 0.8 | 15.0± | 0.2 | 31.2± | 0.6 | 1083生 | 65 |
| 75ppm | 5 | 10.89± | 0.31 | 16.6± | 0.5 | 52. 2± | 1. 4 | 47.9± | 0.4 | 15.2± | 0.2 | 31.7± | 0.5 | 1027± | 87 |
| 150ppm | 5 | 10.69± | 0.34* | 16.0± | 0.4 | 50.7± | 1.7* | 47.4± | 0.5 | 15.0± | 0, 2 | 31.7± | 0.3 | 999土 | 53 |
| 300ppm | 4 | 10.31± | 0, 38** | 15.5± | 0.8** | 48.6± | 2.1** | 47.2± | 0, 7 | 15.0± | 0.2 | 31.8± | 0. 2 | 1146± | 26 |
| 600ppm | 0 | - | | | | - | | - | | - | | - | | - | |

(HCL070)

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1 SEX : FEMALE

REPORT TYPE : A1

HEMATOLOGY (SUMMARY) ALL ANIMALS (3W)

PAGE: 4 Group Name NO. of WBC Differential WBC (%) $10^{8}/\mu$ l Animals N-BAND N-SEG EOSINO BASO MONO LYMPHO OTHER Control 1.80 ± 0.62 $0\pm$ $12\pm$ 2 $1\pm$ 1 0± 0 $1\pm$ 1 87± 3 $0\pm$ 0 38ppm 2.08± 1.42 4 1± 1 $13\pm$ 2 $2\pm$ 3 $0\pm$ 0 $2\pm$ 1 83± 4 $0\pm$ 0 5 75ppm 0.98 ± 0.54 $0\pm$ 11± 3 $2\pm$ 1 Ο± 0 $3\pm$ 3 84± 4 0± 0 150ppm 5 0.55 ± 0.39 $0\pm$ 0 16± 8 $0\pm$ 1 $0\pm$ 0 $1\pm$ $83\pm$ 0± 0 300 ppm0.93± 0.63 $1\pm$ 2 $31 \pm$ 10 $1\pm$ 1 $0\pm$ 0 $2\pm$ 2 66± 12** 0± 0 600ppm Significant difference; $*: P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett (HCL070)

APPENDIX E 1

BIOCHEMISTRY: SUMMARY, MOUSE: MALE

STUDY NO. : 0412 ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1 SEX : MALE

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (3W)

| oup Name | NO. of Animals | TOTAL F g/dl | PROTEIN | ALBUMIN g/dl | | A/G RAT | 10 | T-BILI mg/dl | | GLUCOSE mg/dl | GLUCOSE mg/dl | | T-CHOLESTEROL mg/dl | | TRIGLYCERIDE mg/dl | |
|----------|-------------------|-----------------|---------|-----------------|------|---------|------|-----------------|-------|------------------|------------------|-----|------------------------|-----|-----------------------|--|
| Control | 5 | 5.3± | 0.1 | 3. 2± | 0.0 | 1.5± | 0.1 | 0.16± | 0.03 | 234± | 38 | 84± | 8 | 19± | 6 | |
| 38ppm | 5 | 5.2± | 0.1 | 3.2± | 0. 1 | 1.7± | 0.0 | 0.15± | 0. 02 | 212± | 26 | 84± | 9 | 18± | 4 | |
| 75ppm | 4 | 5.2± | 0.1 | 3.2± | 0. 1 | 1.6± | 0.1 | 0.17± | 0.02 | 215± | 27 | 81± | 5 | 19± | 4 | |
| 150ppm | 5 | 5.2± | 0. 1 | 3.3± | 0.2 | 1.8± | 0.3 | 0.17± | 0.02 | 188± | 48 | 92± | 7 | 15± | 7 | |
| 300ppm | 5 | 5.1± | 0.2 | 3.2± | 0. 1 | 1.7± | 0.0* | 0.18± | 0.02 | 220± | 44 | 99± | 17 | 14± | 5 | |
| 600ppm | 0 | _ | | - | | - | | - | | - | | - | | _ | • | |

(HCL074)

ANIMAL : MOUSE Crj:BDF1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (3W)

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

PAGE: 2

| coup Name | NO. of Animals | PHOSPHO mg/dl | LIPID | GOT IU/2 | | GPT I U/l | | LDH IU/A | | ALP I U/L | | G-GTP IU/2 | | CPK IU/l | ? |
|-----------|-------------------|------------------|-------|-------------|----|--------------|-----|-------------|----|--------------|----|---------------|---|-------------|----|
| Control | 5 | 181± | 21 | 36± | 1 | 14生 | 1 | 210± | 21 | 251± | 16 | 2± | 2 | 86± | 34 |
| 38ppm | 5 | 181± | 17 | 37± | 3 | 14± | 1 | 206± | 30 | 242± | 12 | 2± | 1 | 81± | 28 |
| 75ppm | 4 | 172± | 17 | 37± | 3 | 15± | 2 | 208± | 28 | 228± | 17 | 2± | 1 | 78± | 42 |
| 150ppm | 5 | 167± | 14 | 37± | 3 | 16± | 2 | 205± | 42 | 253± | 16 | 1± | 1 | 58± | 20 |
| 300ppm | 5 | 129± | 25** | 43± | 6* | 20± | 2** | 233± | 54 | 262± | 24 | 1± | 1 | 62± | 19 |
| 600ppm | 0 | - | | - | | - | | - | | | | - | | - | |

(HCL074)

ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (3W)

SEX : MALE

REPORT TYPE : A1

PAGE: 3

| roup Name | NO. of Animals | UREA NI mg/dl | TROGEN | sodium mEq/1 | | POTASSI mEq/J | | CHLORIDE m Eq / l | | CALCIUM mg/dl | | INORGAN mg/dl | IC PHOSPHORUS |
|-----------|-------------------|------------------|--------|-----------------|---|------------------|-----|----------------------|---|------------------|------|------------------|---------------|
| Control | 5 | 29.5± | 4.8 | 152± | 2 | 4.8± | 0.5 | 117± | 2 | 8.8± | 0.5 | 7.0± | 0.8 |
| 38ppm | 5 | 27.6± | 3. 1 | 152± | 2 | 4.8± | 0.4 | 118± | 1 | 8.9± | 0. 2 | 6.9± | 1.1 |
| 75ppm | 4 | 26.1± | 5. 0 | 151± | 2 | 4.9± | 0.1 | 117± | 2 | 8.9± | 0.3 | 7.0± | 1. 4 |
| 150ppm | 5 | 23.1± | 3.8 | 152± | 3 | 5.0± | 0.5 | . 117± | 4 | 8.8± | 0.3 | 8.0± | 1.0 |
| 300ppm | 5 | 27.0± | 3. 0 | 151± | 2 | 4.5± | 0.5 | 116± | 1 | 8.8± | 0.2 | 7.1± | 0.5 |
| 600ppm | 0 | - | | - | | - | | - | | - | | - | |

(HCL074)

APPENDIX E 2

BIOCHEMISTRY: SUMMARY, MOUSE: FEMALE

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1 SEX : FEMALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (3W)

Group Name NO. of TOTAL PROTEIN ALBUMIN A/G RATIO T-BILIRUBIN GLUCOSE T-CHOLESTEROL TRIGLYCERIDE g/dl Animals g/dl mg/dl mg/dl mg/dl mg/dl Control 5 5.3± 0.1 $3.6 \pm$ 0.1 $2.1\pm$ 0.2 0.16± 0.03 190± 30 75± 9 17± 3 38ppm 5 $5.5 \pm$ 0.3 $3.8 \pm$ 0.2 $2.2\pm$ 0.4 0.16± 0.03 195± 27 $77\pm$ 5 17生 5 75ppm 5 $5.4\pm$ 0.2 $3.6\pm$ 0.1 2.0± 0.1 0.22 ± 0.13 $183 \pm$ 33 75± $14\pm$ 4 150ppm 5 $5.2\pm$ 0.1 $3.5\pm$ 0.1 $2.1\pm$ 0.3 0.17± 0.04 30 $77\pm$ $166 \pm$ 8 14土 б 300ppm $5.1 \pm$ 0.1 $3.4 \pm$ 0.1 1.9± 0.1 0.16± 0.01 $229\pm$ 10 $75\pm$ $18\pm$ 5 600ppm

Significant difference; $*: P \le 0.05$

** : $P \le 0.01$

Test of Dunnett

(HCL074)

BAIS 3

PAGE: 4

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1 SEX: FEMALE

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (3W)

| ıp Name | NO. of Animals | PHOSPHOI mg/dl | LIPID | GOT . I U/l | | GPT IU/l | | LDH I U/J | 2 | ALP IU/L | <u></u> | G-GTP I U/l | | CPK IU/l | PAGE : |
|---------|-------------------|-------------------|-------|----------------|----|-------------|---|--------------|-----|-------------|---------|----------------|---|-------------|--------|
| Control | 5 | 160± | 22 | 48± | 6 | 18生 | 5 | 281± | 59 | 372± | 37 | 1± | 1 | 96± | 28 |
| 38ppm | 5 | 158生 | 14 | 48± | 8 | 17± | 4 | 271± | 138 | 358± | 19 | 1± | 1 | 87± | 52 |
| 75ppm | 5 | 144± | 20 | 51± | 11 | 18± | 3 | 265± | 85 | 364± | 33 | 1± | 1 | 66± | 12 |
| 150ppm | 5 | 138± | 15 | 55± | 21 | 20± | 5 | 314± | 144 | 430± | 29* | 1± | 0 | 136生 | 89 |
| 300ppm | 4 | 125± | 17* | 55± | 6 | 25± | 6 | 219± | 25 | 331± | 18 | 2± | 1 | 56土 | 16 |
| 600ppm | 0 | - | | - | | - | | - | | - | | - | | - | |

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME : 1 SEX : FEMALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (3W)

| oup Name | NO. of Animals | UREA NITRO mg∕dl | OGEN | SODIUM m.Eq/1 | | POTASSI m Eq / J | | CHLORIDE m Eq / l | | CALCIUM mg/dl | | INORGAN mg/dl | TIC PHOSPHORUS |
|----------|-------------------|---------------------|------|------------------|---|---------------------|-----|----------------------|---|------------------|------|------------------|----------------|
| Control | 5 | 28. 2± 3 | 3. 9 | 153± | 2 | 4.4± | 0.6 | 119± | 3 | 9.1± | 0. 2 | 6.5± | 0.9 |
| 38ppm | 5 | 26.4± 3 | 3. 8 | 152± | 2 | 4.7± | 0.7 | 119± | 3 | 9.2± | 0.3 | 6.7± | 0.7 |
| 75ppm | 5 | 26.1± 4 | 1. 1 | 152± | 3 | 4.8± | 0.6 | 118± | 4 | 9.0± | 0.2 | 7.5± | 0.7 |
| 150ppm | 5 | 25, 1± 3 | 3. 7 | 152± | 5 | 4.8± | 0.4 | 118± | 4 | 8.9± | 0, 1 | 7.9± | 0.8 |
| 300ppm | 4 | 24.4± 3 | 3. 5 | 151± | 3 | 4.3± | 0.5 | 115± | 2 | 8.8± | 0.4 | 7.6± | 0.8 |
| 600ppm | 0 | <u></u> | | - | | - | | - | | - | | _ | |

(HCL074)

BAIS 3

PAGE: 6

APPENDIX F 1

GROSS FINDINGS : SUMMARY, MOUSE : MALE
DEAD AND MORIBUND ANIMALS

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 3W)

REPORT TYPE : A1 : MALE SEX

PAGE: 1

| Organ | Findings | Group Name NO. of Animals | Control 0 (%) | 38ppm 0 (%) | 75ppm 0 (%) | 150ppm 0 (%) |
|-------------|----------|------------------------------|---------------|----------------|----------------|-----------------|
| stomach | gas | | - (-) | - (-) | - (-) | - (-) |
| small intes | gas | | - (-) | - (-) | - (-) | - (-) |
| ecum | gas | | - (-) | - (-) | - (-) | - (-) |
| abdominal c | gas | | - (-) | - (-) | - (-) | - (-) |
| | | | | | | |
| (HPT080) | | | | | | BAIS |

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 3W)

REPORT TYPE : A1 SEX : MALE

PAGE : 2

| Organ | Findings | Group Name NO. of Animals | 300ppm 0 (%) | 600ppm 5 (%) |
|-------------|----------|------------------------------|-----------------|-----------------|
| | | | | |
| stomach | gas | | - (-) | 4 (80) |
| small intes | gas | | - (-) | 4 (80) |
| cecum | gas | | - (-) | 2 (40) |
| abdominal c | gas | | - (-) | 2 (40) |
| | | | | |
| (HPT080) | | | | RATS 2 |

APPENDIX F 2

GROSS FINDINGS: SUMMARY, MOUSE: MALE: SACRIFICED ANIMALS

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (3W)

REPORT TYPE : A1

SEX : MALE PAGE: 1

| Organ | Findings | Group Name Cont NO. of Animals 5 (%) | rol 38ppm 5 (%) | 75ppm 5 (%) | 150ppm 5 (%) |
|----------|----------------|---|--------------------|----------------|-----------------|
| thymus | atrophic | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| spleen | black zone | 0 (0) | 1 (20) | 0 (0) | 0 (0) |
| kidney | hydronephrosis | 0 (0) | 0 (0) | 1 (20) | 0 (0) |
| | | | | | |
| (HPT080) | | | | | BAIS 3 |

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY)

REPORT TYPE : A1

SEX : MALE SACRIFICED ANIMALS (3W)

| Organ | Findings | Group Name NO. of Animals | 300ppm 5 (%) | 600ppm 0 (%) | |
|----------|----------------|---------------------------|-----------------|-----------------|--------|
| | | | | | |
| thymus | atrophic | | 1 (20) | - (-) | |
| spleen | black zone | | 0 (0) | - (-) | |
| kidney | hydronephrosis | | 0 (0) | - (-) | |
| | | | | | • |
| (HPT080) | | | | | BAIS 3 |

PAGE: 2

APPENDIX F 3

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE

DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 3W)

REPORT TYPE : A1

: FEMALE SEX

PAGE: 3

| Organ | Findings | Group Name NO. of Animals | Control 0 (%) | 38ppm 0 (%) | 75ppm 0 (%) | 150ppm 0 (%) |
|-------------|----------|------------------------------|--------------------|----------------|----------------|-----------------|
| stomach | gas | | - (-) | - (-) | - (-) | - (-) |
| small intes | gas | | - (-) | - (-) | - (-) | - (-) |
| cecum | gas | | - (-) | - (-) | - (-) | - (-) |
| abdominal c | gas | | - (-) | - (-) | - (-) | - (-) |
| | | | | | | |

(HPT080)

BAIS 3

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 3W)

REPORT TYPE : A1 SEX : FEMALE

Group Name 300ppm 600ppm Organ____ Findings__ NO. of Animals 0 (%) 5 (%) stomach - (-) gas 5 (100) small intes gas - (-) 4 (80) cecum gas - (-) 3 (60) abdominal c gas - (-) 1 (20) (HPT080)

BAIS 3

APPENDIX F 4

GROSS FINDINGS: SUMMARY, MOUSE: FEMALE: SACRIFICED ANIMALS

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (3W)

REPORT TYPE : A1

: FEMALE

PAGE: 3

| Organ | Findings | Group Name NO. of Animals | Control 5 (%) | 38ppm 5 (%) | 75ppm 5 (%) | 150ppm 5 (%) |
|--------|------------|------------------------------|------------------|----------------|----------------|-----------------|
| thymus | atrophic | | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| spleen | black zone | | 0 (0) | 0 (0) | 1 (20) | 0 (0) |

(HPT080)

BAIS 3

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (3W)

REPORT TYPE : A1

: FEMALE SEX

| Organ | Findings | Group Name NO. of Animals | 300ppm 5 (%) | 600ppm 0 (%) | |
|----------|------------|---------------------------|-----------------|-----------------|------|
| thymus | atrophic | | 5 (100) | - (-) | |
| spleen | black zone | | 1 (20) | - (-) | |
| | | | | | |
| (HPT080) | | | | | BAIS |

APPENDIX G 1

ORGAN WEIGHT, ABSOLUTE: SUMMARY, MOUSE: MALE

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : MALE UNIT: g ORGAN WEIGHT: ABSOLUTE (SUMMARY)

SURVIVAL ANIMALS (3W)

Group Name NO. of Body Weight THYMUS ADRENALS TESTES HEART LUNGS Animals Control 5 21.3 ± 1.1 0.046± 0.004 0.011 ± 0.003 0.178± 0.033 0.120± 0.003 0.139± 0.010 5 38ppm 21.0 ± 0.6 0.043 ± 0.007 0.012± 0.003 0.176± 0.021 0.117± 0.010 0.144± 0.010 5 75ppm 20.9 ± 0.3 0.034± 0.003** 0.010 ± 0.002 0.183± 0.016 0.117± 0.009 0.150± 0.012 150ppm 5 19.7± 0.4** $0.026 \pm$ 0.003** 0.010± 0.001 0.179± 0.017 0.112± 0.009 0.140 ± 0.012 300ppm 5 16.4生 0.6** 0.014± 0.004** 0.008± 0.001 0.163 ± 0.025 0.096± 0.005** 0.134± 0.009 600ppm 0

Significant difference ; $*: P \le 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL040)

BAIS 3

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : MALE

SEX : MALE UNIT: g ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (3W)

| Animals | KID | NEYS | SPL | EEN | LIV | ER | BRA | IN | | | | |
|---------|-------------|---|---|---|---|---|---|---|---|---|---|---|
| 5 | 0.341± | 0.007 | 0.036± | 0.004 | 0.928± | 0.042 | 0.440± | 0.014 | | | | |
| 5 | 0.339± | 0.018 | 0.035± | 0.002 | 0.893± | 0. 033 | 0.436± | 0.011 | | | | |
| 5 | 0.367± | 0.076 | 0.038± | 0.005 | 0.875± | 0.044 | 0.435± | 0.021 | | | | |
| 5 | 0.325± | 0.008 | 0.030± | 0.004 | 0.787± | 0.030** | 0.428± | 0.013 | | | | |
| 5 | 0.304± | 0.010** | 0.023± | 0.005** | 0.709± | 0, 037** | 0.415± | 0.016 | | | | |
| 0 | - | | - | | - | | - | | | | | |
| | 5 5 5 | 5 0.339 \pm 5 0.367 \pm 5 0.325 \pm 5 0.304 \pm | 5 0.339± 0.018 5 0.367± 0.076 5 0.325± 0.008 5 0.304± 0.010** | 5 0.339 \pm 0.018 0.035 \pm 5 0.367 \pm 0.076 0.038 \pm 5 0.325 \pm 0.008 0.030 \pm 5 0.304 \pm 0.010** 0.023 \pm | 5 0.339± 0.018 0.035± 0.002 5 0.367± 0.076 0.038± 0.005 5 0.325± 0.008 0.030± 0.004 5 0.304± 0.010** 0.023± 0.005** | 5 0.339± 0.018 0.035± 0.002 0.893± 5 0.367± 0.076 0.038± 0.005 0.875± 5 0.325± 0.008 0.030± 0.004 0.787± 5 0.304± 0.010** 0.023± 0.005** 0.709± | 5 0.339± 0.018 0.035± 0.002 0.893± 0.033 5 0.367± 0.076 0.038± 0.005 0.875± 0.044 5 0.325± 0.008 0.030± 0.004 0.787± 0.030** 5 0.304± 0.010** 0.023± 0.005** 0.709± 0.037** | 5 0.339± 0.018 0.035± 0.002 0.893± 0.033 0.436± 5 0.367± 0.076 0.038± 0.005 0.875± 0.044 0.435± 5 0.325± 0.008 0.030± 0.004 0.787± 0.030** 0.428± 5 0.304± 0.010** 0.023± 0.005** 0.709± 0.037** 0.415± | 5 0.339± 0.018 0.035± 0.002 0.893± 0.033 0.436± 0.011 5 0.367± 0.076 0.038± 0.005 0.875± 0.044 0.435± 0.021 5 0.325± 0.008 0.030± 0.004 0.787± 0.030** 0.428± 0.013 5 0.304± 0.010** 0.023± 0.005** 0.709± 0.037** 0.415± 0.016 | 5 | 5 | 5 0.339 ± 0.018 0.035 ± 0.002 0.893 ± 0.033 0.436 ± 0.011 5 0.367 ± 0.076 0.038 ± 0.005 0.875 ± 0.044 0.435 ± 0.021 5 0.325 ± 0.008 0.030 ± 0.004 0.787 ± 0.030** 0.428 ± 0.013 5 0.304 ± 0.010** 0.023 ± 0.005** 0.709 ± 0.037** 0.415 ± 0.016 0 - - - - - - - |

(HCL040)

BAIS 3

APPENDIX G 2

ORGAN WEIGHT, ABSOLUTE: SUMMARY, MOUSE: FEMALE

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : FEMALE UNIT: g ORGAN WEIGHT: ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (3W)

PAGE: 3

| up Name | NO. of Animals | Body Weight | THYMUS | ADRENALS | OVARIES | HEART | LUNGS | |
|---------|-------------------|-------------|----------------|--------------|----------------|----------------|---------------|--|
| Control | 5 | 17.4± 0.4 | 0.063± 0.004 | 0.011± 0.002 | 0.022± 0.008 | 0.105± 0.008 | 0.134± 0.008 | |
| 38ppm | 5 | 17.2± 0.7 | 0.061± 0.003 | 0.010± 0.001 | 0.019± 0.004 | 0.099± 0.005 | 0.136± 0.003 | |
| 75ppm | 5 | 16.6± 0.7 | 0.049± 0.008** | 0.010± 0.002 | 0.020± 0.002 | 0.097± 0.008 | 0.137± 0.006 | |
| 150ppm | 5 | 15.8± 0.8** | 0.031± 0.006** | 0.009± 0.001 | 0.017± 0.004 | 0.096± 0.005 | 0.127± 0.011 | |
| 300ppm | 5 | 13.3± 0.7** | 0.011± 0.002** | 0.007± 0.000 | 0.011± 0.000** | 0.082± 0.005** | 0.117± 0.009* | |
| 600ppm | 0 | - | - | - | - | - - | - | |

(HCL040)

BAIS 3

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : FEMALE UNIT: g

ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (3W)

| AGE: | |
|------|--|
| | |

| roup Name | NO. of Animals | KID | NEYS | SPL | EEN | LIV | ER . | BRA | I.N | | |
|-----------|-------------------|--------|--------|--------|---------|--------|---------|--------|---------|--|--|
| Control | 5 | 0.250± | 0.011 | 0.045± | 0,001 | 0.762± | 0.061 | 0.449± | 0. 012 | | |
| 38ppm | 5 | 0.246± | 0.009 | 0.040± | 0.002 | 0.747± | 0.033 | 0.443± | 0.011 | | |
| 75ppm | 5 | 0.257± | 0.011 | 0.038± | 0.006 | 0.722± | 0. 023 | 0.445± | 0.008 | | |
| 150ppm | 5 | 0.243± | 0.008 | 0.032± | 0.007* | 0.650± | 0.049** | 0.425± | 0.014* | | |
| 300ppm | 5 | 0.231± | 0.008* | 0.024± | 0.006** | 0.615± | 0.041** | 0.398± | 0.011** | | |
| 600ppm | 0 | - | | - | | - | | - | | | |

(HCL040)

BAIS 3

APPENDIX H 1

ORGAN WEIGHT, RELATIVE: SUMMARY, MOUSE: MALE

STUDY NO. : 0412 ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : MALE UNIT: %

ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (3W)

PAGE: 1

| oup Name | NO. of Animals | Body Weight (g) | THYMUS | ADRENALS | TESTES | HEART | LUNGS | |
|----------|-------------------|-----------------|----------------|--------------|--------------|--------------|----------------|--|
| Control | 5 | 21.3± 1.1 | 0.216± 0.010 | 0.053± 0.013 | 0.835± 0.139 | 0.564± 0.026 | 0.655± 0.043 | |
| 38ppm | 5 | 21.0± 0.6 | 0.204± 0.027 | 0.055± 0.012 | 0.839± 0.086 | 0.557± 0.033 | 0.686± 0.036 | |
| 75ppm | 5 | 20.9± 0.3 | 0.165± 0.016** | 0.049± 0.010 | 0.875± 0.076 | 0.559± 0.037 | 0.717± 0.048 | |
| 150ppm | 5 | 19.7± 0.4** | 0.132± 0.017** | 0.049± 0.006 | 0.906± 0.091 | 0.571± 0.053 | 0.712± 0.068 | |
| 300ppm | 5 | 16.4± 0.6** | 0.086± 0.023** | 0.048± 0.010 | 1.001± 0.178 | 0.589± 0.039 | 0.817± 0.073** | |
| 600ppm | 0 | - | - | - | - | | - | |

(HCL042)

BAIS 3

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (3W)

SEX : MALE UNIT: %

| up Name | NO. of Animals | KIDNEYS | SPLEEN | LIVER | BRAIN | |
|---------|-------------------|----------------|--------------|----------------|----------------|--|
| Control | 5 | 1.602± 0.082 | 0.168± 0.012 | 4.361± 0.091 | 2.073± 0.165 | |
| 38ppm | 5 | 1.618± 0.058 | 0.165± 0.008 | 4.262± 0.040 | 2.084± 0.111 | |
| 75ppm | 5 | 1.761± 0.365 | 0.182± 0.023 | 4.193± 0.144 | 2.086± 0.086 | |
| 150ppm | 5 | 1.649± 0.021 | 0.153± 0.021 | 3.990± 0.161** | 2.173± 0.055 | |
| 300ppm | 5 | 1.856± 0.084** | 0.144± 0.035 | 4.330 ± 0.142 | 2.537± 0.084** | |
| 600ppm | 0 | - | | - | - | |

(HCL042)

BAIS 3

APPENDIX H 2

ORGAN WEIGHT, RELATIVE: SUMMARY, MOUSE: FEMALE

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : FEMALE UNIT: %

ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (3W)

| p Name | NO. of Animals | Body Weight (g) | THYMUS | ADRENALS | OVARIES | HEART | LUNGS | |
|---------|-------------------|-----------------|----------------|--------------|--------------|--------------|----------------|--|
| Control | 5 | 17.4± 0.4 | 0.363± 0.030 | 0.061± 0.009 | 0.127± 0.042 | 0.605± 0.049 | 0.769± 0.045 | |
| 38ppm | 5 | 17.2± 0.7 | 0.357± 0.028 | 0.057± 0.010 | 0.113± 0.022 | 0.578± 0.041 | 0.793± 0.042 | |
| 75ppm | 5 | 16.6± 0.7 | 0.293± 0.045** | 0.058± 0.014 | 0.121± 0.012 | 0.583± 0.036 | 0.825± 0.008 | |
| 150ppm | 5 | 15.8± 0.8** | 0.193± 0.032** | 0.058± 0.009 | 0.106± 0.017 | 0.607± 0.034 | 0.800± 0.037 | |
| 300ppm | 5 | 13.3± 0.7** | 0.084生 0.012** | 0.053± 0.003 | 0.081± 0.005 | 0.617± 0.025 | 0.880± 0.048** | |
| 600ppm | 0 | _ | _ | _ | - | - | - | |

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : FEMALE UNIT: %

ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (3W)

| oup Name | NO. of Animals | KIDNEYS | SPLEEN | LIVER | BRAIN | |
|----------|-------------------|----------------|----------------|--------------|----------------|--|
| Control | 5 | 1.435± 0.046 | 0.256± 0.005 | 4.373± 0.339 | 2.576± 0.071 | |
| 38ppm | 5 | 1.435± 0.087 | 0.232± 0.015 | 4.351± 0.085 | 2.586± 0.107 | |
| 75ppm | 5 | 1.550± 0.127 | 0.227± 0.031 | 4.352± 0.156 | 2.686± 0.075 | |
| 150ppm | 5 | 1.541± 0.104 | 0.201± 0.033** | 4.116± 0.251 | 2.700± 0.188 | |
| 300ppm | 5 | 1.744± 0.045** | 0.177± 0.037** | 4.632± 0.172 | 2.999± 0.150** | |
| 600ppm | 0 | - | - | - - | _ | |

(HCL042)

BAIS 3

APPENDIX I 1

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: MALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0412 ANIMAL : MOUSE Crj:BDF1 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 3W)

DEAD AND MORIBUND ANIMALS (0-

REPORT TYPE : A1

SEX : MALE

| Organ | Findings | Group Name Control No. of Animals on Study 0 Grade 1 2 3 4 (%) (%) (%) (%) | 38ppm 0 1 2 3 4 (%) (%) (%) (%) | 75ppm 0 1 2 3 4 (%) (%) (%) | 150ppm 0 1 2 3 4 (%) (%) (%) (%) |
|---------------------|---|---|--|--------------------------------------|---|
| {Respiratory | system) | | - | | |
| nasal cavit | -,, | ⟨ 0⟩ | < 0> . | < 0> | < 0> |
| | exudate | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) |
| | inflammation:respiratory epithelium | (-) (-) (-) (-) | (-) (-) (-) (· -) | (-) (-) (-) (-) | (-) (-) (-) (-) |
| | necrosis:olfactory epithelium | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) |
| | necrosis:respiratory epithelium | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) |
| nasopharynx | necrosis:epithelium | < 0> | < 0> | < 0> | < 0> |
| | Mediasis.epitMetium | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) |
| larynx | necrosis:epithelium | < 0> | < 0> | < 0> | < 0> |
| | necrosis.epitnerium | (-) (-) (-) (-) | < 0> (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) |
| trachea | manusis turid 12. | < 0> | < 0> | < 0> | < 0> |
| | necrosis:epithelium | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) |
| Grade < a > b (c) | 1 : Slight 2 : Moderate a : Number of animals examined at the b : Number of animals with lesion c : b / a * 100 | 3 : Marked 4 : Severe site | | | |
| (HPT150) | | | | | DATCO |

STUDY NO. : 0412 ANIMAL : MOUSE

: MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : MALE HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 3W)

PAGE: 2 Group Name 300ppm 600ppm No. of Animals on Study 5 Organ___ Findings_ (%) (%) (%) {Respiratory system} nasal cavit exudate (-) (-) (-) (0)(40)(0)(0) inflammation:respiratory epithelium (-) (-) (-) (60) (0) (0) (0) necrosis:olfactory epithelium (-) (-) (-) (0)(20)(80)(0) necrosis:respiratory epithelium (-) (-) (-) (-) (0)(0)(100) nasopharynx < 0> < 5> necrosis:epithelium (-) (-) (-) (60) (0) (0) (0) larynx < 5> necrosis:epithelium (-) (-) (-) (20) (0) (80) (0) trachea < 0> < 5> necrosis:epithelium (-) (-) (-) (-) (0)(20)(80)(0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe < a > a : Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a*100

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 3W)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : MALE

| Organ | No | oup Name Control of Animals on Study 0 ade 1 2 3 4 (%) (%) (%) (%) | 38ppm 0 1 2 3 4 (%) (%) (%) (%) | 75ppm 0 1 2 3 4 (%) (%) (%) (%) | 150ppm 0 0 15(%) (%) (%) (%) (%) |
|-----------------|--|--|--|--|----------------------------------|
| {Respiratory | system} | | | | |
| lung | necrosis:epithelium, bronchus | (-) (-) (-) (-) | (-) (-) (-) (-) | < 0> (-) (-) (-) (-) | (-) (-) (-) (-) |
| {Hematopoiet | ic system) | | | | |
| thymus | atrophy | (-) (-) (-) (-) | < 0> (-) (-) (-) (-) | < 0> (-) (-) (-) (-) | (-) (-) (-) (-) |
| | karyorrhexis | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) | (-) (-) (-) (-) |
| {Reproductiv | e system} | | | | |
| əpididymis | decreased:sperma | < 0> (-) (-) (-) (-) | < 0> (-) (-) (-) (-) | < 0> (-) (-) (-) (-) | < 0> (-) (-) (-) (-) |
| | debris of spermatic elements | (-) (-) (-) (-) | (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) |
| Grade (a) b (c) | 1: Slight 2: Moderate 3: a: Number of animals examined at the site b: Number of animals with lesion c: b/a*100 | Marked 4 : Severe | | | |

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 3W)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

SEX : MALE

| Organ | Group No. o Grade Findings | f Animals on Study 0 | 600ppm 5 1 2 3 4 (%) (%) (%) (%) | |
|---------------------|---|---------------------------------|---|--|
| {Respiratory | system} | | | |
| lung | necrosis:epithelium, bronchus | (-) (-) (-) (-) | < 5> 1 | |
| {Hematopoiet | ic system} | | | |
| thymus | atrophy | < 0> (-) (-) (-) (-) | < 5> 0 3 1 0 (0) (60) (20) (0) | |
| | karyorrhexis | (-) (-) (-) | 3 1 1 0 (60) (20) (20) (0) | |
| {Reproductiv | re system) | | | |
| epididymis | decreased:sperma | < 0> (-) (-) (-) (-) | <pre></pre> | |
| | debris of spermatic elements | | 0 1 0 0 (0) (20) (0) (0) | |
| Grade < a > b (c) | 1: Slight 2: Moderate 3: Mar a: Number of animals examined at the site b: Number of animals with lesion c: b/a*100 | ked 4 : Severe | | |

(HPT150)

APPENDIX I 2

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: MALE: SACRIFICED ANIMALS

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (3W)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : MALE

| Organ | No | oup Name of Animals on Study ade 1 (%) | 2 (%) | Contro 3 (%) | 4 (%) | <u>1</u> (%) | 2 (%) | 38r 5 3 (%) | 9pm 4 (%) | 1 (%) | (| 5 <u>2</u> %) | 75pp 3 (%) | m <u>4</u> (%) | 1 (%) | 2 (% | 5 : | 150ppm 3 (%) | m 4 (%) |
|--------------|--|--|-----------|--------------------|--------|--------------|--------|----------------------|-----------|------------|---|---------------------|------------------|----------------|------------|--------|-----------|--------------------|---------------|
| (Respiratory | system) | | | | | | | | | | | | | | | | | | |
| asal cavit | exudate , | 0 (0) | 0 (0) | 0 | 0 (0) | 0 (0) | 0 | 5> 0 (0) | 0 (0) | 0 (0) | (| < 52 0 0) (|) 0 0) (| 0 () | 1 (20) | 0 | | 0 0) (| 0 0) |
| | inflammatory polyp | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 3 (60) | | 0 0) (| 0 | 0 () | 5 (100) | 0) | | 0 (| 0 |
| | inflammation:respiratory epithelium | 0 (0) | 0 (0) | 0 (0) | 0 | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | (| 0 0) (| 0 | 0 (0) | 0 (0) | (0 |)) (| 0 (| 0 |
| | respiratory metaplasia:olfactory epithel | ium 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 4 (80) | (| 0 | 0 | 0 (0) | 4 (80) | 1 (20 | | 0 (| 0 |
| | squamous cell motaplasia:respiratory epi | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | (| 0 0) (| 0 | 0 (0) | 0 (0) | | | 0 (| 0 |
| | sclerosis:lamina propria | 0 (0) | 0 (0) | 0 (0) | 0 | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | (| 0 0) (| 0 | 0 (0) | 1 (20) | ((|))) (| 0 (| 0 |
| | atrophy:olfactory epithelium | 0 (0) | 0 (0) | 0 (0) | 0 | 0 (0) | 0 (0) | 0 (0) | 0 (0) . | 4 (80) | | 0 0) (| 0 | 0 | 2 (40) | (60 | | 0 (| 0 |
| | necrosis:olfactory epithelium | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (40) | (| 0 0) (| 0 | 0 | 4 (80) | ((| | 0 (| 0 |

<a>>

a : Number of animals examined at the site

b

b : Number of animals with lesion

(c)

c:b/a*100

(HPT150)

BAIS3

ANIMAL : MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (3W)

REPORT TYPE : A1 SEX : MALE

| 0rgan | 1 | Group Name No. of Animals on Study Grade 1 (%) | 300ppm 5 2 3 4 (%) (%) (%) | 600ppm 0 1 2 3 4 (%) (%) (%) | · |
|---------------------|---|--|-------------------------------------|---------------------------------------|---|
| {Respiratory | system) | | | | |
| nasal cavit | exudate | 0 (0) | < 5> 0 4 0 (0) (80) (0) | < 0> (-) (-) (-) (-) | |
| | inflammatory polyp | 5 (100) | 0 0 0 0 (0) (0) | (-) (-) (-) | |
| | inflammation:respiratory epithelium | 1 (20) | 0 0 0 0 (0) (0) | (-) (-) (-) | |
| | respiratory metaplasia:olfactory epith | elium 3 (60) | 2 0 0 (40) (0) (0) | (-) (-) (-) (-) | |
| | squamous cell metaplasia:respiratory e | pithelium 0 (0) | 5 0 0 (100) (0) (0) | (-) (-) (-) (-) | |
| | sclerosis:lamina propria | 3 (60) | 0 0 0 0 (0) (0) | (-) (-) (-) (-) | |
| | atrophy:olfactory epithelium | 1 (20) | 2 2 0 (40) (40) (0) | (-) (-) (-) (-) | |
| | necrosis:olfactory epithelium | 5 (100) | 0 0 0 0 (0) (0) | (-) (-) (-) (-) | |
| Grade < a > b (c) | 1: Slight 2: Moderate 3 a: Number of animals examined at the si b: Number of animals with lesion c: b / a * 100 | : Marked 4 : Sever te | re | | |

(HPT150)

STUDY NO. : 0412 ANIMAL : MOUSI HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

: MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : MALE SACRIFICED ANIMALS (3W)

Group Name Control 38ppm 75ppm 150ppm No. of Animals on Study 5 5 5 Grade Organ___ Findings_ {Respiratory system} nasal cavit < 5> < 5> < 5> degeneration:respiratory epithelium 0 0 0 4 1 (0)(0)(0)(0) (20) (60) (0) (0) (0)(80)(20)(0) (0)(40)(60)(0) necrosis:respiratory epithelium 5 (0)(0)(0)(0) (0)(0)(0)(0) (60) (0) (0) (0) (100) (0) (0) (0) nasopharynx < 5> < 5> < 5> < 5> degeneration:epithelium 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) necrosis:epithelium (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) trachea < 5> degeneration:epithelium 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) {Hematopoietic system} thymus < 5> < 5> atrophy 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe (a) a: Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a*100

(HPT150)

BAIS3

ANIMAL : MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (3W)

REPORT TYPE : A1

SEX : MALE

| Organ | 1 | Froup Name 300p No. of Animals on Study 5 Frade 1 2 3 (%) (%) (%) | | 600ppm 0 3 4 (%) (%) | | |
|---------------------|---|--|---------------------|-------------------------------|--|--|
| {Respiratory | system} | | | · | | |
| nasal cavit | degeneration:respiratory epithelium | < 5> 2 3 0 (40) (60) (0) | | 0> (-) (-) | | |
| | necrosis:respiratory epithelium | 0 5 0 (0) (100) (0) | 0 (0) (-) (-) | (-) (-) | | |
| nasopharynx | degeneration:epithelium | <pre></pre> | 0 (0) (-) (-) | 0> (-) (-) | | |
| | necrosis:epithelium | 3 0 0 (60)(0)(0) | 0 (0) (-) (-) | (-) (-) | | |
| trachea | degeneration:epithelium | <pre></pre> | 0 | 0> (-) (-) | | |
| {Hematopoieti | c system) | | | | | |
| thymus | atrophy | 1 0 0 (20) (0) (0) | | 0> | | |
| Grade < a > b (c) | 1: Slight 2: Moderate 3 a: Number of animals examined at the si b: Number of animals with lesion c: b / a * 100 | : Marked 4 : Severe te | | | | |

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

: MOUSE Crj:BDF1 SACRIFICED ANIMALS (3W)

REPORT TYPE : A1 SEX : MALE

ANIMAL

PAGE: 5 Group Name Control 150ppm No. of Animals on Study 5 5 Grade Findings_ (%) (%) (%) (%) (%) (%) {Hematopoietic system} spleen < 5> < 5> deposit of melanin 0 0 0 0 (0)(0)(0)(0) (20) (0) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) {Circulatory system} heart < 5> < 5> lymphocytic infiltration 0 0 0 0 (0)(0)(0)(0) (20) (0) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) {Urinary system} kidney < 5> < 5> < 5> hydronephrosis 0 0 0 0 1 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(20)(0)(0) (0)(0)(0)(0) {Endocrine system} pituitary < 5> < 5> Rathke pouch 0 0 0 0 0 0 (0)(0)(0)(0) (20) (0) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) 1 : Slight Grade 2 : Moderate 3 : Marked 4 : Severe (a) a : Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a*100

(HPT150)

(HPT150)

ANIMAL : MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (3W)

REPORT TYPE : A1

: MALE SEX

| Organ | Findings | Group Name No. of Animals on Study Grade 1 (%) | 30 5 (%) (% | | 600ppm 0 1 2 3 4 (%) (%) (%) (%) | |
|---------------------|--|--|-------------------------|---------|---|--|
| {Hematopoiet | tic system) | | | | | |
| spleen | deposit of melanin | 0 (0) | < 5> 0 ((0) (0 | 0 (0) | < 0> (-) (-) (-) (-) | |
| {Circulatory | / system} | | | | | |
| heart . | lymphocytic infiltration | 0 (0) | < 5> 0 ((0) ((| 0) (0) | < 0> (-) (-) (-) (-) | |
| {Urinary sys | etem) | | | | | |
| kidney | hydronephrosis | 0 (0) | < 5> 0 ((0) ((| 0 (0) | < 0> (-) (-) (-) (-) | |
| {Endocrine s | system} | | | | | |
| pituitary | Rathke pouch | 0 (0) | < 5> 0 ((0) (0 | 0) (0) | < 0> (-) (-) (-) (-) | |
| Grade < a > b (c) | 1: Slight 2: Moderate a: Number of animals examined at the b: Number of animals with lesion c: b/a*100 | 3 : Marked 4 : Severe site | • | | | |

BAIS3

APPENDIX I 3

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: FEMALE: DEAD AND MORIBUND ANIMALS

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 3W)

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX : FEMALE

| Organ | Findings | Group Name Control No. of Animals on Study 0 Grade 1 2 3 4 (%) (%) (%) (%) (%) | 38ppm 0 1 2 3 4 (%) (%) (%) (%) | 75ppm 0 1 2 3 4 (%) (%) (%) (%) | 150ppm 0 1 2 3 4 (%) (%) (%) (%) |
|---------------------|--|--|--|--|---|
| {Respiratory | system) | | | | |
| nasal cavit | | < 0> | < 0> | < 0> | < 0> |
| | exudate | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) |
| | inflammation:respiratory epithelium | (-) (-) (-) (-) | (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) |
| | necrosis:olfactory epithelium | (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) |
| | necrosis:respiratory epithelium | (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) |
| nasopharynx | | < 0> | < 0> | < 0> | < 0> |
| | necrosis:epithelium | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) |
| larynx | | < 0> | < 0> | < 0> | < 0> |
| | necrosis:epithelium | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) |
| trachea | | < 0> | < 0> | < 0> | < 0> |
| | necrosis:epithelium | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) |
| Grade (a > b (c) | 1: Slight 2: Moderate a: Number of animals examined at the b: Number of animals with lesion c: b/a * 100 | 3 : Marked 4 : Severe site | | | |

ANIMAL : MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0- 3W)

REPORT TYPE : A1 : FEMALE SEX

| Organ | Findings | Group Name | 300ppm 0 2 3 4 (%) (%) | 600ppm 5 1 2 3 4 (%) (%) (%) (%) | |
|--------------|-------------------------------------|-------------------------|---------------------------------|---|--|
| {Respiratory | system) | | | | |
| nasal cavit | exudate | (-) (| < 0> -) (-) (-) | <pre></pre> | |
| | inflammation:respiratory epithelium | . (-) (| | 3 0 0 0 0 (60) (60) (60) | |
| | necrosis:olfactory epithelium | (-) (| -) (-) (-) | 0 0 5 0 (0) (100) (0) | |
| | necrosis:respiratory epithelium | (-) (| -) (-) (-) | 0 0 0 5 (0) (0) (100) | |
| nasopharynx | necrosis:epithelium | (-) (| | <pre></pre> | |
| larynx | necrosis:epithelium | - (-) (| < 0> -) (-) (-) | <pre></pre> | |
| trachea | necrosis:epithelium | _ (-) (| | <pre></pre> | |

(HPT150)

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 3W)

PAGE: 7

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX

: FEMALE

| Organ | Group Nam No. of An Grade | e Control imals on Study 0 | 38ppm 0 1 2 3 4 (%) (%) (%) (%) | 75ppm 0 1 2 3 4 (%) (%) (%) (%) | 150ppm 0 1 2 3 4 (%) (%) (%) (%) |
|------------------------------|---|---------------------------------|--|--|---|
| {Hematopoi | etic system) | | | | |
| thymus | atrophy | < 0> (-) (-) (-) (-) | < 0> (-) (-) (-) (-) | < 0> (-) (-) (-) (-) | (-) (-) (-) (-) |
| | karyorrhexis | (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) | (-) (-) (-) (-) |
| Grade < a > b (c) | 1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 | 4 : Severe | | | · · · · · · · · · · · · · · · · · · · |

ANIMAL

SEX

: MOUSE Crj:BDF1

REPORT TYPE : A1 : FEMALE HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 3W)

Group Name 300ppm 600ppm No. of Animals on Study Grade (%) Findings_ Organ____ {Hematopoietic system} thymus < 0> < 5> atrophy 0 3 1 0 (-) (-) (-) (-) (0)(60)(20)(0) karyorrhexis 0 2 1 0 (-) (-) (-) (-) (0) (40) (20) (0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe (a) a : Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a*100 (HPT150) BAIS3

APPENDIX I 4

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: FEMALE: SACRIFICED ANIMALS

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (3W)

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1

SEX

: FEMALE

Group Name Control 38ppm 75ppm 150ppm No. of Animals on Study 5 5 5 Grade Organ_ Findings_ {Respiratory system} nasal cavit < 5> < 5> < 5> < 5> exudate 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) inflammatory polyp 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (80) (0) (0) (0) (80) (0) (0) (0) inflammation:respiratory epithelium 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) respiratory metaplasia:olfactory epithelium (0)(0)(0)(0) (0)(0)(0)(0) (100) (0) (0) (0) (100) (0) (0) (0) squamous cell metaplasia:respiratory epithelium 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) sclerosis: lamina propria 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (40) (0) (0) (0) atrophy:olfactory epithelium (0)(0)(0)(0) (0)(0)(0)(0) (80) (20) (0) (0) (20) (80) (0) (0) necrosis:olfactory epithelium 5 (0)(0)(0)(0) (0)(0)(0)(0) (40) (0) (0) (0) (100) (0) (0) (0) Grade 1 : Slight 2 : Moderate 3 : Marked

4 : Severe

< a >

b

(c)

a: Number of animals examined at the site

b: Number of animals with lesion

c:b/a*100

: MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (3W)

ANIMAL REPORT TYPE : A1

SEX : FEMALE

| Organ | Findings | Group Name No. of Animals on Stud Grade | 1 2 (%) (%) | 300ppm 5 3 4 (%) (%) | 1 2 (%) (% | 600ppm 0 3 4) (%) (% | <u>, , , , , , , , , , , , , , , , , , , </u> |
|---------------------|--|---|------------------|-------------------------------|---|--------------------------------|---|
| {Respiratory | system) | | | | | | |
| nasal cavit | exudate | (| 0 0 0 0) (0) | 5> 5 0 (100) (0) | | < 0> - (-) (- |) |
| | inflammatory polyp | (1 | 5 0 100) (0) | 0 0 | - (-) (- | | · •) |
| | inflammation:respiratory epithelium | (| 2 0 40) (0) | 0 0 | (-) (- | · | - -) |
| | respiratory metaplasia:olfactory epi | thelium (| 0 5 0)·(100) | 0 0 | (-) (- | | - -) |
| | squamous coll metaplasia:respiratory | | 0 5 0) (100) | 0 0 (0) | (-) (- | -) (-) (- | - -) |
| | sclerosis:lamina propria | (| 5 0 100) (0) | 0 0 (0) | - · · · · · · · · · · · · · · · · · · · | -) (₋ -) (- | - -) |
| | atrophy:olfactory epithelium | (| 0 3 0) (60) | 2 0 (40) (0) | (-) (· | | - -) |
| | necrosis:olfactory epithelium | (| 4 1 80) (20) | 0 0 (0) | (-) (- | -) (<u>-</u>) (- | - -) |
| Grade < a > b (c) | 1: Slight 2: Moderate a: Number of animals examined at the b: Number of animals with lesion c: b / a * 100 | 3: Marked 4: S site | evere | | | | · |

(HPT150)

: MOUSE Crj:BDF1 ANIMAL

REPORT TYPE : A1 SEX : FEMALE HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (3W)

PAGE: 9 Group Name Control 38ppm 75ppm 150ppm No. of Animals on Study 5 5 Organ_ Findings_ (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) {Respiratory system} nasal cavit < 5> < 5> degeneration:respiratory epithelium 0 0 2 0 0 (0)(0)(0)(0) (0)(100)(0)(0) (0)(60)(40)(0) (0)(0)(100)(0) necrosis:respiratory epithelium 0 0 5 (0)(0)(0)(0) (0)(0)(0)(0) (100) (0) (0) (0) (100) (0) (0) (0) nasopharynx < 5> < 5> < 5> < 5> degeneration: epithelium 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) necrosis:epithelium 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) larynx < 5> < 5> < 5> < 5> degeneration: epithelium 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) necrosis:epithelium (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) trachea < 5> < 5> < 5> < 5> degeneration: epithelium 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe (a) a: Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a*100

ANIMAL

SEX

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

: MOUSE Cri:BDF1

REPORT TYPE : A1

: FEMALE

SACRIFICED ANIMALS (3W)

Group Name 300ppm 600ppm No. of Animals on Study Organ___ Findings_ {Respiratory system} nasal cavit < 5> degeneration:respiratory epithelium 0 5 0 0 (0) (100) (0) (0) (-) (-) (-) necrosis:respiratory epithelium (-) (-) (-) (0)(100)(0)(0) nasopharynx < 5> < 0> degeneration:epithelium 0 0 5 0 (0) (0) (100) (0) (-) (-) (-) necrosis:epithelium (80) (20) (0) (0) (-) (-) (-) larynx < 5> degeneration:epithelium 0 0 1 0 (-) (-) (-) (0)(0)(20)(0) necrosis:epithelium (20) (0) (0) (0) (-) (-) (-) trachea < 5> < 0> degeneration:epithelium 0 2 3 0 (0)(40)(60)(0) (-) (-) (-) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe (a) a: Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a*100

(HPT150)

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (3W)

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1 SEX : FEMALE

| Organ | | p Name | 38ppm 5 1 2 3 4 (%) (%) (%) (%) | 75ppm 5 1 2 3 4 (%) (%) (%) (%) | 150ppm 5 1 2 3 4 (%) (%) (%) |
|--------------------------|--|--|--|---------------------------------|--|
| {Hematopoiet | cic system) | | | | |
| thymus | atrophy | 0 0 0 0 (0) (0) (0) (0) | (5) 0 0 0 0 (0) (0) (0) (0) | <pre></pre> | < 5> 0 0 0 0 (0) (0) (0) (0) |
| spleen | deposit of melanin | < 5> 0 0 0 0 (0) (0) (0) (0) | < 5> 0 0 0 0 (0) (0) (0) (0) | <pre></pre> | <pre></pre> |
| (Digestive s | system) | | | | |
| tomach | cyst | < 5> 0 0 0 0 (0) (0) (0) (0) | (5) 1 0 0 0 (20) (0) (0) (0) | <pre></pre> | (55) 1 |
| | erosion:forestomach | 0 0 0 0 0 (0) (0) | 0 0 0 0 0 (0) (0) | 1 0 0 0 (20) (0) (0) (0) | 0 1 0 0 (0) (20) (0) (0) |
| | hyperplasia:forestomach | 0 0 0 0 0 (0) (0) | 0 0 0 0 0 (0) (0) | 1 0 0 0 0 (20) (0) (0) | 0 0 0 0 0 (0) (0) |
| liver | granulation | 5> 1 0 0 0 (20) (0) (0) (0) | 1 0 0 0 (20) (0) (0) (0) | 2 0 0 0 (40) (0) (0) (0) | <pre></pre> |
| Grade (a) b (c) | 1: Slight 2: Moderate 3: Ma a: Number of animals examined at the site b: Number of animals with lesion c: b/a*100 | rked 4 : Severe | | | |

SEX : FEMALE

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (3W)

| Organ | | Group Name 300ppm No. of Animals on Study 5 Grade 1 2 3 4 (%) (%) (%) (%) | 600ppm 0 1 2 3 4 (%) (%) (%) (%) | |
|-------------------------|--|---|---|---|
| {Hematopoiet | ic system) | | | |
| thymus | atrophy | < 5> 4 1 0 0 (80) (20) (0) (0) | < 0> (-) (-) (-) (-) | |
| spleen | deposit of melanin | < 5> 1 0 0 0 (20) (0) (0) (0) | < 0> (-) (-) (-) (-) | |
| {Digestive s | ystem} | | | |
| stomach | cyst | < 5> 0 0 0 0 (0) (0) (0) (0) | < 0> (-) (-) (-) (-) | |
| | erosion:forestomach | 0 0 0 0 0 (0) (0) | (-) (-) (-) | |
| | hyperplasia:forestomach | 0 0 0 0 0 (0) (0) | (-) (-) (-) | · |
| liver | granulation | <pre></pre> | < 0> (-) (-) (-) (-) | • |
| Grade <a>> b (c) | 1: Slight 2: Moderate 3 a: Number of animals examined at the s b: Number of animals with lesion c: b/a * 100 | : Marked 4 : Severe ite | | |

STUDY NO. : 0412 ANIMAL

: MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (3W)

REPORT TYPE : A1

SEX : FEMALE

Group Name Control 38ppm 75ppm 150ppm No. of Animals on Study Grade (%) Organ____ Findings_ (%) {Endocrine system} parathyroid < 4> < 3> < 3> cyst 0 0 0 0 0 0 0 0 0 (0) (0) (0) (0) (33) (0) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) {Reproductive system} vagina < 5> < 5> mucification:epithelium 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) 1 : Slight Grade 2 : Moderate 3 : Marked 4 : Severe (a) a: Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a * 100 (HPT150) BAIS3

: MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (3W)

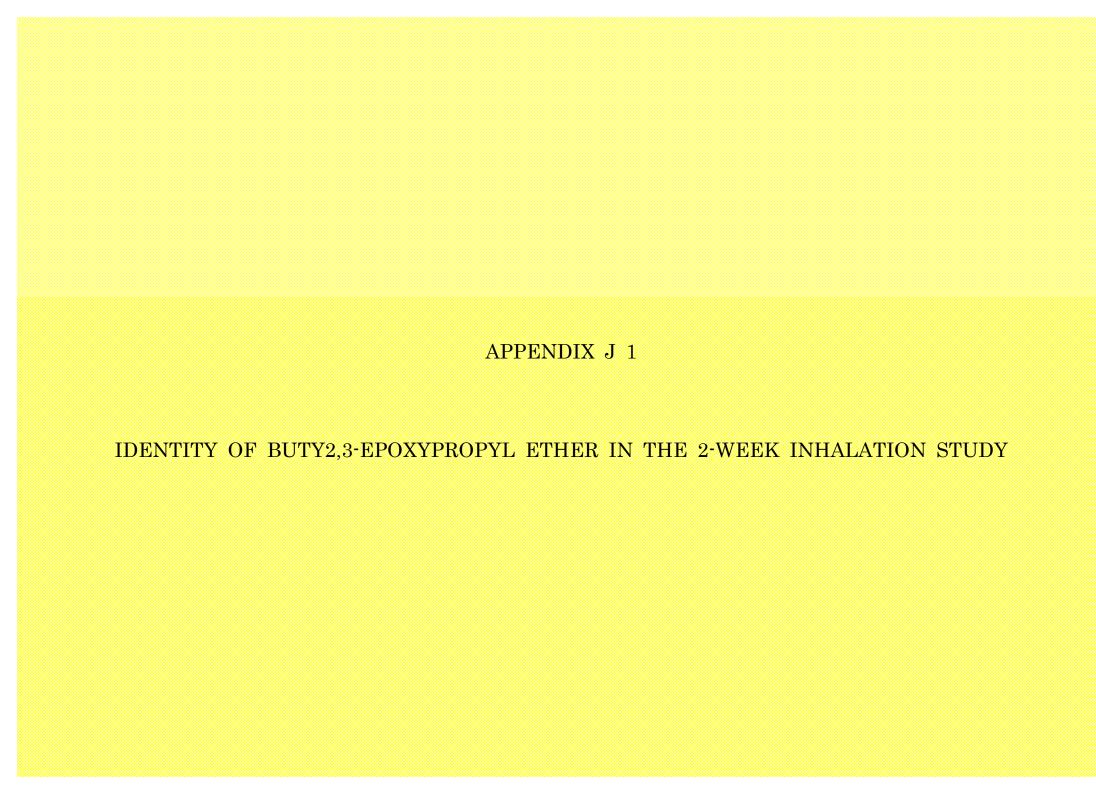
ANIMAL REPORT TYPE : A1

(HPT150)

SEX : FEMALE

Group Name 300ppm 600ppm No. of Animals on Study Grade Findings_ (%) Organ____ {Endocrine system} parathyroid < 2> < 0> cyst (-) (-) (-) (-) (0)(0)(0)(0) {Reproductive system} vagina < 5> < 0> mucification:epithelium 2 0 0 (40) (40) (0) (0) (-) (-) (-) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe < a > a: Number of animals examined at the site b: Number of animals with lesion b (c) c:b/a*100

BAIS3



IDENTITY OF BUTYL 2,3-EPOXYPROPYL ETHER IN THE 2-WEEK INHALATION STUDY

Test Substance: Butyl 2,3-epoxypropyl ether (Wako Pure Chemical Industries, Ltd.)

Lot No. : CHK5928

1. Spectral Data

Mass Spectrometry

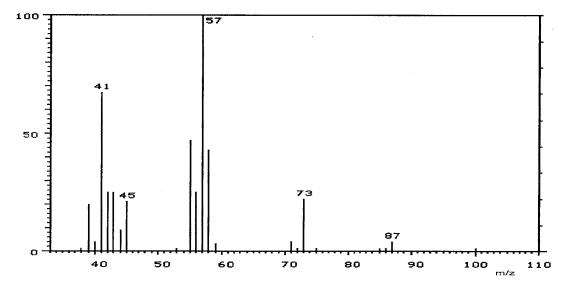
Instrument

: Hitachi M-80B Mass Spectrometer

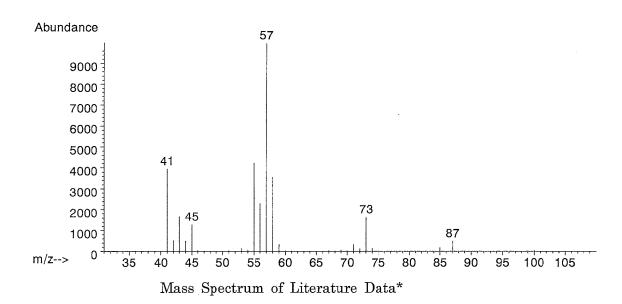
Ionization

: EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Result: The mass spectrum was consistent with literature spectrum.

(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition.

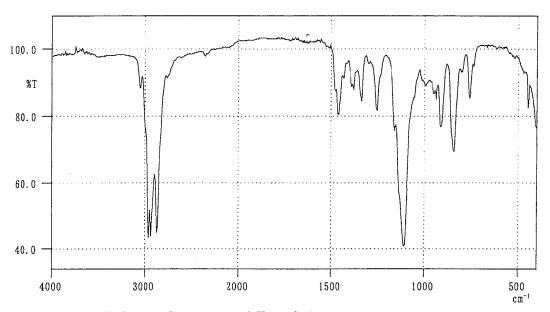
John Wiley and Sons, Inc. (U.S.), Entry Number 20313)

Infrared Spectrometry

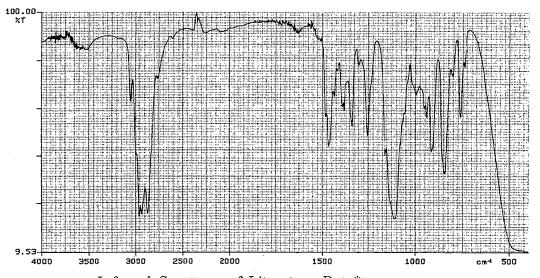
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm⁻¹



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

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

2. Conclusion: The test substance was identified as butyl 2,3-epoxypropyl ether by mass spectrum and infrared spectrum.

| APPENDIX J 2 |
|---|
| STABILITY OF BUTY2,3-EPOXYPROPYL ETHER IN THE 2-WEEK INHALATION STUDY |
| |
| |

STABILITY OF BUTYL 2,3-EPOXYPROPYL ETHER IN THE 2-WEEK INHALATION STUDY

Test Substance: Butyl 2,3-epoxypropyl ether (Wako Pure Chemical Industries, Ltd.)

Lot No.

: CHK5928

1. Sample

: This lot was used from 2000.3.28 to 2000.4.10. Test substance was stored

in a dark place at room temperature.

2. Gas Chromatography

Instrument

: Hewlett Packard 5890A Gas Chromatograph

Column

: Methyl Silicone (0.53 mm $\phi \times 60$ m)

Column Temperature: 160° C

Flow Rate

: 20 mL/min

Detector

)

: FID (Flame Ionization Detector)

Injection Volume

: 1 µL

| Date (date analyzed) | Peak No. | Retention Time (min) | Area (%) |
|-------------------------|----------|----------------------|-------------|
| 2000.03.24 | 1 | 2.850 | 100 |
| 2000.04.26 | 1 | 2.851 | 100 |

Result: Gas chromatography indicated one major peak (peak No.1) analyzed on 2000.3.24 and one major peak (peak No.1) analyzed on 2000.4.26. No new trace impurity peak in the test substance analyzed on 2000.4.26 was detected.

3. Conclusion: The test substance was stable for about 1 month in a dark place at room temperature.

APPENDIX K 1

CONCENTMOUSEION OF BUTY2,3-EPOXYPROPYL ETHER
IN THE INHALATION CHAMBER
OF 2-WEEK INHALATION STUDY

CONCENTRATION OF BUTYL 2,3-EPOXYPROPYL ETHER IN THE INHALATION CHAMBER OF THE 2-WEEK INHALATION STUDY

| Group Name | Concentration(ppm) $Mean \pm S.D.$ | | |
|---------------|---------------------------------------|---|-----|
| 0ppm(Control) | 0.0 | ± | 0.0 |
| 38ppm | 38.4 | ± | 0.5 |
| 75ppm | 75.5 | ± | 0.5 |
| 150ppm | 151.3 | ± | 1.3 |
| 300ppm | 301.4 | ± | 2.4 |
| 600ppm | 600.0 | ± | 1.8 |

APPENDIX K 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-WEEK INHALATION STUDY OF BUTY2,3-EPOXYPROPYL ETHER

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2 -WEEK INHALATION SYUDY OF BUTYL 2,3-EPOXYPROPYL ETHER

| Group Name | Temperature(°C) Mean \pm S.D. | Humidity(%) Mean \pm S.D. | Ventilation Rate(L/min) Mean \pm S.D. | Air Change(time/h) Mean |
|-------------------|------------------------------------|--------------------------------|--|----------------------------|
| 0ppm(Control) | 21.9 ± 0.2 | 52.9 ± 4.4 | 104.4 ± 0.4 | 12.0 |
| 38ppm | 22.2 ± 0.2 | 47.9 ± 5.7 | 104.3 ± 0.3 | 12.0 |
| $75 \mathrm{ppm}$ | 22.1 ± 0.1 | 46.3 ± 6.0 | 104.7 ± 0.3 | 12.1 |
| 150ppm | 21.9 ± 0.2 | 47.7 ± 7.6 | 104.5 ± 0.4 | 12.1 |
| 300ppm | 21.8 ± 0.1 | 46.2 ± 7.7 | 104.4 ± 0.3 | 12.0 |
| 600ppm | 21.6 ± 0.3 | 43.0 ± 0.3 | 104.4 ± 0.2 | 12.0 |

APPENDIX L 1

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK INHALATION STUDY OF BUTY2,3-EPOXYPROPYL ETHER

METHOD FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK INHALATION STUDY OF BUTYL 2,3-EPOXYPROPYL ETHER

| Item | Method |
|--|---|
| Hematology | |
| Red blood cell (RBC) | Light scattering method 1) |
| Hemoglobin (Hgb) | Cyanmethemoglobin method 1) |
| Hematocrit (Hct) | Calculated as RBC × MCV/10 1) |
| Mean corpuscular volume (MCV) | Light scattering method 1) |
| Mean corpuscular hemoglobin (MCH) | Calculated as Hgb/RBC × 10 1) |
| Mean corpuscular hemoglobin concentration (MCHC) | Calculated as Hgb/Hct × 100 1) |
| Platelet | Light scattering method 1) |
| White blood cell (WBC) | Light scattering method 1) |
| Differential WBC | Pattern recognition method 2) |
| | (Wright staining) |
| Biochemistry | |
| Total protein (TP) | Biuret method ³⁾ |
| Albumin (Alb) | BCG method 3) |
| A/G ratio | Calculated as Alb/(TP-Alb) 3) |
| T-bilirubin | Alkaline azobilirubin method 3) |
| Glucose | GlcK·G-6-PDH method 3) |
| T-cholesterol | CE·COD·POD method 3) |
| Triglyceride | LPL·GK·GPO·POD method 3) |
| Phospholipid | PLD·ChOD·POD method 3) |
| Glutamic oxaloacetic transaminase (GOT) | JSCC method 3) |
| Glutamic pyruvic transaminase (GPT) | JSCC method 3) |
| Lactate dehydrogenase (LDH) | SFBC method 3) |
| Alkaline phosphatase (ALP) | GSCC method 3) |
| γ -Glutamyl transpeptidase (γ -GTP) | L- γ -Glutamyl-p-nitroanilide method ³⁾ |
| Creatine phosphokinase (CPK) | JSCC method 3) |
| Urea nitrogen | Urease • GLDH method 3) |
| Sodium | Ion selective electrode method 3) |
| Potassium | Ion selective electrode method 3) |
| Chloride | Ion selective electrode method 3) |
| Calcium | OCPC method 3) |
| Inorganic phosphorus | PNP·XOD·POD method 3) |

- 1) Automatic blood cell analyzer (Technicon H·1: Bayer Corporation)
- 2) Automatic blood cell differential analyzer (MICROX HEG-120NA: OMRON Corporation)
- 3) Automatic analyzer (Hitachi 7070: Hitachi, Ltd.)

APPENDIX L 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK INHALATION STUDY OF BUTY2,3-EPOXYPROPYL ETHER

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK INHALATION STUDY OF BUTYL 2,3—EPOXYPROPYL ETHER

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