| | |
|---|---|
| **C Number:** | C60902B |
| **Lock Date:** | Not Entered. |
| **Cage Range:** | All |
| **Date Range:** | All |
| **Reasons For Removal:** | All |
| **Removal Date Range:** | All |
| **Treatment Groups:** | All |
| **Study Gender:** | Both |
| **PWG Approval Date** | NONE |

## HISTORICAL CONTROL STUDIES
## From NA 1994 report

### SAME ROUTE

05106-03 -- Diethyl phthalate (SKIN ACETONE)
05109-12 -- Triethanolamine (SKIN ACETONE)

### ALL ROUTES

05085-02 -- Manganese sulfate monohydrate (ORAL FEED)
05086-02 -- o-Benzyl-p-chlorophenol (GAVAGE CORN OIL)
05087-03 -- Triamterene (ORAL FEED)
05089-02 -- Chloraminated water (ORAL WATER)
05090-02 -- Coumarin (GAVAGE CORN OIL)
05091-02 -- 3,4-Dihydrocoumarin (GAVAGE CORN OIL)
05092-02 -- o-Nitroanisole (ORAL FEED)
05093-01 -- p-Nitroaniline (GAVAGE CORN OIL)
05100-04 -- Tricresyl phosphate (ORAL FEED)
05101-01 -- Methyl bromide (INHALATION AIR)
05102-06 -- Benzethonium chloride (SKIN ETHANOL)
05106-03 -- Diethyl phthalate (SKIN ACETONE)
05108-02 -- Promethazine hydrochloride (GAVAGE WATER)
05109-12 -- Triethanolamine (SKIN ACETONE)
05111-02 -- 1,2,3-Trichloropropane (GAVAGE CORN OIL)
05114-02 -- Hexachlorocyclopentadiene (INHALATION AIR)
05120-04 -- Benzyl acetate (ORAL FEED)
05127-02 -- Barium chloride dihydrate (ORAL WATER)
05130-02 -- C.I. Direct blue 218 (ORAL FEED)
05131-02 -- Sodium fluoride (ORAL WATER)
05133-04 -- Acetonitrile (INHALATION AIR)
05134-02 -- 1,3-Butadiene (INHALATION AIR)
05142-04 -- tert-Butyl alcohol (ORAL WATER)
05150-02 -- Methylphenidate hydrochloride (ORAL FEED)
05155-04 -- p-Nitrobenzoic acid (ORAL FEED)
05165-02 -- 4,4-Thiobis(6-tert-butyl-m-cresol) (ORAL FEED)
05185-04 -- Isobutyl nitrite (INHALATION AIR)

## HISTORICAL CONTROL STUDIES
## From NA 1994 report

05212-03 -- Oxazepam (ORAL FEED)
05214-02 -- 1-trans-delta-9-Tetrahydrocannabinol (GAVAGE CORN OIL)
88034-04 -- Ozone (INHALATION AIR)

**FOR ALL DOSES THE TUMOR RATES IN THE FOLLOWING TISSUES/ORGANS ARE BASED ON NUMBER OF TISSUES IN OTHER TISSUES/ORGANS RATES ARE BASED ON THE NUMBER OF ANIMALS NECROPSIED.**

Liver
Lung
Pituitary Gland

## SUMMARY OF STATISTICALLY SIGNIFICANT (P<=.05) RESULTS IN THE ANALYSIS OF 1,2-DIHYDRO-2,2,4-

**MALE MOUSE**

| Organ | Morphology |
|---|---|
| Liver | Hepatocellular Carcinoma |
| Lung | Alveolar/Bronchiolar Adenoma |
| | Alveolar/Bronchiolar Carcinoma or Alveolar/Bronchiolar Adenoma |

**FEMALE MOUSE**

| Organ | Morphology |
|---|---|
| Pituitary Gland: Pars Distalis or Unspecified Site | Adenoma |
| Uterus | Sarcoma Stromal |
| | Sarcoma Stromal or Polyp Stromal |
| All Organs | Benign Tumors |
| | Malignant and Benign Tumors |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 104 WEEKS

| | MALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **Liver** | | | |
| **Hepatocellular Adenoma** | | | |
| **TUMOR RATES** | | | |
| **OVERALL(a)** | 3/15 (20%) | 5/13 (38%) | 4/14 (29%) |
| **POLY-3 RATE (b)** | 3/9.15 | 5/8.83 | 4/8.77 |
| **POLY-3 PERCENT (g)** | 32.8% | 56.6% | 45.6% |
| **INT SACRIFICE 1** | 3/10 (30%) | 1/10 (10%) | 4/10 (40%) |
| **TERMINAL (d)** | 0/0 (0%) | 0/0 (0%) | 0/1 (0%) |
| **FIRST INCIDENCE** | 463(I) | 463(I) | 316 |
| **HC TUMORS SAME ROUTE** | 33/100 (33%) | | |
| **HC TUMORS ALL ROUTES** | 625/1554 (40%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | P=0.346 | P=0.276 | P=0.470 |
| **POLY 1.5** | P=0.349 | P=0.265 | P=0.463 |
| **POLY 6** | P=0.353 | P=0.308 | P=0.493 |
| **COCH-ARM / FISHERS** | P=0.350 | P=0.255 | P=0.458 |
| **MAX-ISO-POLY-3** | P=0.283 | P=0.137 | P=0.278 |
| **HISTCONT SAME RTE** | P=0.470 | P=0.402 | P=0.461 |
| **HISTCONT ALL RTES** | P=0.551 | P=0.412 | P=1.000 |
| **CURR VS HC SAME RTE** | P=0.981 | | |
| **CURR VS HC ALL RTES** | P=0.663 | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 104 WEEKS

| | MALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **Liver** | | | |
| **Hepatocellular Carcinoma** | | | |
| **TUMOR RATES** | | | |
| **OVERALL(a)** | 3/15 (20%) | 2/13 (15%) | 0/14 (0%) |
| **POLY-3 RATE (b)** | 3/8.64 | 2/7.48 | 0/6.89 |
| **POLY-3 PERCENT (g)** | 34.7% | 26.7% | 0% |
| **INT SACRIFICE 1** | 0/10 (0%) | 0/10 (0%) | 2/10 (20%) |
| **TERMINAL (d)** | 0/0 (0%) | 0/0 (0%) | 0/1 (0%) |
| **FIRST INCIDENCE** | 428 | 463(I) | --- |
| **HC TUMORS SAME ROUTE** | 19/100 (19%) | | |
| **HC TUMORS ALL ROUTES** | 317/1554 (20%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | P=0.121N | P=0.580N | P=0.127N |
| **POLY 1.5** | P=0.115N | P=0.573N | P=0.124N |
| **POLY 6** | P=0.138N | P=0.605N | P=0.135N |
| **COCH-ARM / FISHERS** | P=0.106N | P=0.572N | P=0.125N |
| **MAX-ISO-POLY-3** | P=0.082N | P=0.364N | P=0.047N* |
| **HISTCONT SAME RTE** | P=1.000 | P=0.500 | P=1.000 |
| **HISTCONT ALL RTES** | P=1.000 | P=1.000 | P=1.000 |
| **CURR VS HC SAME RTE** | P=0.455 | | |
| **CURR VS HC ALL RTES** | P=0.442 | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 104 WEEKS

| | MALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **Liver** | | | |
| **Hepatocellular Carcinoma or Hepatocellular Adenoma** | | | |
| **TUMOR RATES** | | | |
| **OVERALL(a)** | 6/15 (40%) | 6/13 (46%) | 4/14 (29%) |
| **POLY-3 RATE (b)** | 6/10.38 | 6/9.41 | 4/8.77 |
| **POLY-3 PERCENT (g)** | 57.8% | 63.8% | 45.6% |
| **INT SACRIFICE 1** | 3/10 (30%) | 1/10 (10%) | 5/10 (50%) |
| **TERMINAL (d)** | 0/0 (0%) | 0/0 (0%) | 0/1 (0%) |
| **FIRST INCIDENCE** | 428 | 463(I) | 316 |
| **HC TUMORS SAME ROUTE** | 40/100 (40%) | | |
| **HC TUMORS ALL ROUTES** | 814/1554 (52%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | P=0.448N | P=0.585 | P=0.468N |
| **POLY 1.5** | P=0.413N | P=0.548 | P=0.432N |
| **POLY 6** | P=0.519N | P=0.675 | P=0.549N |
| **COCH-ARM / FISHERS** | P=0.379N | P=0.521 | P=0.400N |
| **MAX-ISO-POLY-3** | P=0.345N | P=0.380 | P=0.290N |
| **HISTCONT SAME RTE** | P=0.530 | P=0.398 | P=1.000 |
| **HISTCONT ALL RTES** | P=0.681 | P=0.454 | P=1.000 |
| **CURR VS HC SAME RTE** | P=0.499 | | |
| **CURR VS HC ALL RTES** | P=0.813 | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 104 WEEKS

| | MALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **Liver** | | | |
| **Hepatocellular Carcinoma, Hepatocellular Adenoma, or Hepatoblastoma** | | | |
| **TUMOR RATES** | | | |
| **OVERALL(a)** | 6/15 (40%) | 6/13 (46%) | 4/14 (29%) |
| **POLY-3 RATE (b)** | 6/10.38 | 6/9.41 | 4/8.77 |
| **POLY-3 PERCENT (g)** | 57.8% | 63.8% | 45.6% |
| **INT SACRIFICE 1** | 3/10 (30%) | 1/10 (10%) | 5/10 (50%) |
| **TERMINAL (d)** | 0/0 (0%) | 0/0 (0%) | 0/1 (0%) |
| **FIRST INCIDENCE** | 428 | 463(I) | 316 |
| **HC TUMORS SAME ROUTE** | 40/100 (40%) | | |
| **HC TUMORS ALL ROUTES** | 815/1554 (52%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | P=0.448N | P=0.585 | P=0.468N |
| **POLY 1.5** | P=0.413N | P=0.548 | P=0.432N |
| **POLY 6** | P=0.519N | P=0.675 | P=0.549N |
| **COCH-ARM / FISHERS** | P=0.379N | P=0.521 | P=0.400N |
| **MAX-ISO-POLY-3** | P=0.345N | P=0.380 | P=0.290N |
| **HISTCONT SAME RTE** | P=0.530 | P=0.398 | P=1.000 |
| **HISTCONT ALL RTES** | P=0.682 | P=0.455 | P=1.000 |
| **CURR VS HC SAME RTE** | P=0.499 | | |
| **CURR VS HC ALL RTES** | P=0.816 | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 104 WEEKS

| | MALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **Lung** | | | |
| **Alveolar/Bronchiolar Adenoma** | | | |
| **TUMOR RATES** | | | |
| **OVERALL(a)** | 3/15 (20%) | 1/13 (8%) | 0/14 (0%) |
| **POLY-3 RATE (b)** | 3/8.57 | 1/6.44 | 0/6.89 |
| **POLY-3 PERCENT (g)** | 35% | 15.5% | 0% |
| **INT SACRIFICE 1** | 2/10 (20%) | 0/10 (0%) | 0/10 (0%) |
| **TERMINAL (d)** | 0/0 (0%) | 0/0 (0%) | 0/1 (0%) |
| **FIRST INCIDENCE** | 463(I) | 592 | --- |
| **HC TUMORS SAME ROUTE** | 20/100 (20%) | | |
| **HC TUMORS ALL ROUTES** | 297/1555 (19%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | P=0.073N | P=0.395N | P=0.125N |
| **POLY 1.5** | P=0.071N | P=0.369N | P=0.122N |
| **POLY 6** | P=0.077N | P=0.481N | P=0.133N |
| **COCH-ARM / FISHERS** | P=0.070N | P=0.356N | P=0.125N |
| **MAX-ISO-POLY-3** | P=0.058N | P=0.212N | P=0.046N* |
| **HISTCONT SAME RTE** | (h) | (h) | (h) |
| **HISTCONT ALL RTES** | (h) | (h) | (h) |
| **CURR VS HC SAME RTE** | P=0.477 | | |
| **CURR VS HC ALL RTES** | P=0.388 | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 104 WEEKS

| | MALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **Lung** | | | |
| **Alveolar/Bronchiolar Carcinoma or Alveolar/Bronchiolar Adenoma** | | | |
| **TUMOR RATES** | | | |
| **OVERALL(a)** | 3/15 (20%) | 1/13 (8%) | 0/14 (0%) |
| **POLY-3 RATE (b)** | 3/8.57 | 1/6.44 | 0/6.89 |
| **POLY-3 PERCENT (g)** | 35% | 15.5% | 0% |
| **INT SACRIFICE 1** | 2/10 (20%) | 0/10 (0%) | 0/10 (0%) |
| **TERMINAL (d)** | 0/0 (0%) | 0/0 (0%) | 0/1 (0%) |
| **FIRST INCIDENCE** | 463(I) | 592 | --- |
| **HC TUMORS SAME ROUTE** | 24/100 (24%) | | |
| **HC TUMORS ALL ROUTES** | 380/1555 (24%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | P=0.073N | P=0.395N | P=0.125N |
| **POLY 1.5** | P=0.071N | P=0.369N | P=0.122N |
| **POLY 6** | P=0.077N | P=0.481N | P=0.133N |
| **COCH-ARM / FISHERS** | P=0.070N | P=0.356N | P=0.125N |
| **MAX-ISO-POLY-3** | P=0.058N | P=0.212N | P=0.046N* |
| **HISTCONT SAME RTE** | (h) | (h) | (h) |
| **HISTCONT ALL RTES** | (h) | (h) | (h) |
| **CURR VS HC SAME RTE** | P=0.613 | | |
| **CURR VS HC ALL RTES** | P=0.613 | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 104 WEEKS

| | MALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **Pituitary Gland: Pars Distalis or Unspecified Site** | | | |
| **Adenoma** | | | |
| **TUMOR RATES** | # | # | # |
| **OVERALL(a)** | 0/15 (0%) | 0/13 (0%) | 0/14 (0%) |
| **POLY-3 RATE (b)** | 0/7.40 | 0/6.32 | 0/6.89 |
| **POLY-3 PERCENT (g)** | 0% | 0% | 0% |
| **INT SACRIFICE 1** | 0/10 (0%) | 0/10 (0%) | 0/10 (0%) |
| **TERMINAL (d)** | 0/0 (0%) | 0/0 (0%) | 0/1 (0%) |
| **FIRST INCIDENCE** | --- | --- | --- |
| **HC TUMORS SAME ROUTE** | 0/96 (0%) | | |
| **HC TUMORS ALL ROUTES** | 7/1460 (0%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | (n) | (n) | (n) |
| **POLY 1.5** | (n) | (n) | (n) |
| **POLY 6** | (n) | (n) | (n) |
| **COCH-ARM / FISHERS** | (n) | (n) | (n) |
| **MAX-ISO-POLY-3** | (n) | (n) | (n) |
| **HISTCONT SAME RTE** | (n) | (n) | (n) |
| **HISTCONT ALL RTES** | (n) | (n) | (n) |
| **CURR VS HC SAME RTE** | (n) | | |
| **CURR VS HC ALL RTES** | (n) | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 104 WEEKS

| | MALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **All Organs** | | | |
| **Benign Tumors** | | | |
| **TUMOR RATES** | # | # | # |
| **OVERALL(a)** | 6/15 (40%) | 6/13 (46%) | 6/14 (43%) |
| **POLY-3 RATE (b)** | 6/10.32 | 6/8.95 | 6/9.93 |
| **POLY-3 PERCENT (g)** | 58.1% | 67% | 60.4% |
| **INT SACRIFICE 1** | 5/10 (50%) | 3/10 (30%) | 4/10 (40%) |
| **TERMINAL (d)** | 0/0 (0%) | 0/0 (0%) | 0/1 (0%) |
| **FIRST INCIDENCE** | 463(I) | 463(I) | 316 |
| **HC TUMORS SAME ROUTE** | 51/100 (51%) | | |
| **HC TUMORS ALL ROUTES** | 926/1556 (60%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | P=0.555 | P=0.533 | P=0.653 |
| **POLY 1.5** | P=0.530 | P=0.526 | P=0.615 |
| **POLY 6** | P=0.629 | P=0.563 | P=0.739 |
| **COCH-ARM / FISHERS** | P=0.513 | P=0.521 | P=0.587 |
| **MAX-ISO-POLY-3** | P=0.530 | P=0.325 | P=0.453 |
| **HISTCONT SAME RTE** | P=0.523 | P=0.440 | P=0.474 |
| **HISTCONT ALL RTES** | P=0.660 | P=0.498 | P=1.000 |
| **CURR VS HC SAME RTE** | P=0.782 | | |
| **CURR VS HC ALL RTES** | P=0.867 | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 104 WEEKS

| | MALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **All Organs** | | | |
| **Malignant Tumors** | | | |
| **TUMOR RATES** | # | # | # |
| **OVERALL(a)** | 4/15 (27%) | 4/13 (31%) | 1/14 (7%) |
| **POLY-3 RATE (b)** | 4/8.74 | 4/7.79 | 1/7.12 |
| **POLY-3 PERCENT (g)** | 45.8% | 51.3% | 14% |
| **INT SACRIFICE 1** | 0/10 (0%) | 0/10 (0%) | 2/10 (20%) |
| **TERMINAL (d)** | 0/0 (0%) | 0/0 (0%) | 0/1 (0%) |
| **FIRST INCIDENCE** | 428 | 463(I) | 566 |
| **HC TUMORS SAME ROUTE** | 38/100 (38%) | | |
| **HC TUMORS ALL ROUTES** | 598/1556 (38%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | P=0.211N | P=0.619 | P=0.190N |
| **POLY 1.5** | P=0.205N | P=0.588 | P=0.190N |
| **POLY 6** | P=0.214N | P=0.735 | P=0.184N |
| **COCH-ARM / FISHERS** | P=0.192N | P=0.569 | P=0.186N |
| **MAX-ISO-POLY-3** | P=0.108N | P=0.400 | P=0.088N |
| **HISTCONT SAME RTE** | P=1.000 | P=0.331 | P=1.000 |
| **HISTCONT ALL RTES** | P=1.000 | P=0.434 | P=1.000 |
| **CURR VS HC SAME RTE** | P=0.734 | | |
| **CURR VS HC ALL RTES** | P=0.757 | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 104 WEEKS

| | MALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **All Organs** | | | |
| **Malignant and Benign Tumors** | | | |
| **TUMOR RATES** | # | # | # |
| **OVERALL(a)** | 9/15 (60%) | 7/13 (54%) | 6/14 (43%) |
| **POLY-3 RATE (b)** | 9/11.65 | 7/9.53 | 6/9.93 |
| **POLY-3 PERCENT (g)** | 77.3% | 73.5% | 60.4% |
| **INT SACRIFICE 1** | 5/10 (50%) | 3/10 (30%) | 5/10 (50%) |
| **TERMINAL (d)** | 0/0 (0%) | 0/0 (0%) | 0/1 (0%) |
| **FIRST INCIDENCE** | 428 | 463(I) | 316 |
| **HC TUMORS SAME ROUTE** | 66/100 (66%) | | |
| **HC TUMORS ALL ROUTES** | 1184/1556 (76%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | P=0.264N | P=0.650N | P=0.325N |
| **POLY 1.5** | P=0.259N | P=0.575N | P=0.308N |
| **POLY 6** | P=0.281N | P=0.860N | P=0.371N |
| **COCH-ARM / FISHERS** | P=0.249N | P=0.521N | P=0.291N |
| **MAX-ISO-POLY-3** | P=0.227N | P=0.403N | P=0.169N |
| **HISTCONT SAME RTE** | P=0.675 | P=0.488 | P=1.000 |
| **HISTCONT ALL RTES** | (h) | (h) | (h) |
| **CURR VS HC SAME RTE** | P=0.542 | | |
| **CURR VS HC ALL RTES** | P=1.000 | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 105 WEEKS

| | FEMALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **Liver** | | | |
| **Hepatocellular Adenoma** | | | |
| **TUMOR RATES** | | | |
| **OVERALL(a)** | 3/19 (16%) | 1/13 (8%) | 5/17 (29%) |
| **POLY-3 RATE (b)** | 3/10.49 | 1/7.71 | 5/11.06 |
| **POLY-3 PERCENT (g)** | 28.6% | 13% | 45.2% |
| **INT SACRIFICE 1** | 1/10 (10%) | 4/10 (40%) | 1/10 (10%) |
| **TERMINAL (d)** | 0/1 (0%) | 0/1 (0%) | 0/0 (0%) |
| **FIRST INCIDENCE** | 462(I) | 462(I) | 462(I) |
| **HC TUMORS SAME ROUTE** | 26/100 (26%) | | |
| **HC TUMORS ALL ROUTES** | 393/1553 (25%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | P=0.294 | P=0.410N | P=0.355 |
| **POLY 1.5** | P=0.301 | P=0.401N | P=0.354 |
| **POLY 6** | P=0.275 | P=0.443N | P=0.347 |
| **COCH-ARM / FISHERS** | P=0.262 | P=0.458N | P=0.281 |
| **MAX-ISO-POLY-3** | P=0.169 | P=0.221N | P=0.212 |
| **HISTCONT SAME RTE** | P=0.493 | P=1.000 | P=0.403 |
| **HISTCONT ALL RTES** | P=0.461 | P=1.000 | P=0.344 |
| **CURR VS HC SAME RTE** | P=0.971 | | |
| **CURR VS HC ALL RTES** | P=0.912 | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 105 WEEKS

| | FEMALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **Liver** | | | |
| **Hepatocellular Carcinoma** | | | |
| **TUMOR RATES** | | | |
| **OVERALL(a)** | 1/19 (5%) | 1/13 (8%) | 0/17 (0%) |
| **POLY-3 RATE (b)** | 1/9.40 | 1/7.14 | 0/8.78 |
| **POLY-3 PERCENT (g)** | 10.6% | 14% | 0% |
| **INT SACRIFICE 1** | 0/10 (0%) | 0/10 (0%) | 0/10 (0%) |
| **TERMINAL (d)** | 0/1 (0%) | 1/1 (100%) | 0/0 (0%) |
| **FIRST INCIDENCE** | 605 | 612 | --- |
| **HC TUMORS SAME ROUTE** | 5/100 (5%) | | |
| **HC TUMORS ALL ROUTES** | 184/1553 (12%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | (n) | (n) | (n) |
| **POLY 1.5** | (n) | (n) | (n) |
| **POLY 6** | (n) | (n) | (n) |
| **COCH-ARM / FISHERS** | (n) | (n) | (n) |
| **MAX-ISO-POLY-3** | (n) | (n) | (n) |
| **HISTCONT SAME RTE** | (n) | (n) | (n) |
| **HISTCONT ALL RTES** | (n) | (n) | (n) |
| **CURR VS HC SAME RTE** | (n) | | |
| **CURR VS HC ALL RTES** | (n) | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 105 WEEKS

| | | FEMALE | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **Liver** | | | |
| **Hepatocellular Carcinoma or Hepatocellular Adenoma** | | | |
| **TUMOR RATES** | | | |
| **OVERALL(a)** | 4/19 (21%) | 2/13 (15%) | 5/17 (29%) |
| **POLY-3 RATE (b)** | 4/10.53 | 2/7.71 | 5/11.06 |
| **POLY-3 PERCENT (g)** | 38% | 25.9% | 45.2% |
| **INT SACRIFICE 1** | 1/10 (10%) | 4/10 (40%) | 1/10 (10%) |
| **TERMINAL (d)** | 0/1 (0%) | 1/1 (100%) | 0/0 (0%) |
| **FIRST INCIDENCE** | 462(I) | 462(I) | 462(I) |
| **HC TUMORS SAME ROUTE** | 30/100 (30%) | | |
| **HC TUMORS ALL ROUTES** | 510/1553 (33%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | P=0.475 | P=0.484N | P=0.542 |
| **POLY 1.5** | P=0.470 | P=0.467N | P=0.524 |
| **POLY 6** | P=0.474 | P=0.545N | P=0.560 |
| **COCH-ARM / FISHERS** | P=0.396 | P=0.530N | P=0.423 |
| **MAX-ISO-POLY-3** | P=0.385 | P=0.295N | P=0.366 |
| **HISTCONT SAME RTE** | P=0.528 | P=1.000 | P=0.430 |
| **HISTCONT ALL RTES** | P=0.575 | P=1.000 | P=0.438 |
| **CURR VS HC SAME RTE** | P=0.802 | | |
| **CURR VS HC ALL RTES** | P=0.852 | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 105 WEEKS

| | FEMALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **Liver** | | | |
| **Hepatocellular Carcinoma, Hepatocellular Adenoma, or Hepatoblastoma** | | | |
| **TUMOR RATES** | | | |
| **OVERALL(a)** | 4/19 (21%) | 2/13 (15%) | 5/17 (29%) |
| **POLY-3 RATE (b)** | 4/10.53 | 2/7.71 | 5/11.06 |
| **POLY-3 PERCENT (g)** | 38% | 25.9% | 45.2% |
| **INT SACRIFICE 1** | 1/10 (10%) | 4/10 (40%) | 1/10 (10%) |
| **TERMINAL (d)** | 0/1 (0%) | 1/1 (100%) | 0/0 (0%) |
| **FIRST INCIDENCE** | 462(I) | 462(I) | 462(I) |
| **HC TUMORS SAME ROUTE** | 30/100 (30%) | | |
| **HC TUMORS ALL ROUTES** | 510/1553 (33%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | P=0.475 | P=0.484N | P=0.542 |
| **POLY 1.5** | P=0.470 | P=0.467N | P=0.524 |
| **POLY 6** | P=0.474 | P=0.545N | P=0.560 |
| **COCH-ARM / FISHERS** | P=0.396 | P=0.530N | P=0.423 |
| **MAX-ISO-POLY-3** | P=0.385 | P=0.295N | P=0.366 |
| **HISTCONT SAME RTE** | P=0.528 | P=1.000 | P=0.430 |
| **HISTCONT ALL RTES** | P=0.575 | P=1.000 | P=0.438 |
| **CURR VS HC SAME RTE** | P=0.802 | | |
| **CURR VS HC ALL RTES** | P=0.852 | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 105 WEEKS

| | FEMALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **Lung** | | | |
| **Alveolar/Bronchiolar Adenoma** | | | |
| **TUMOR RATES** | | | |
| **OVERALL(a)** | 0/19 (0%) | 1/13 (8%) | 0/17 (0%) |
| **POLY-3 RATE (b)** | 0/9.37 | 1/7.18 | 0/8.78 |
| **POLY-3 PERCENT (g)** | 0% | 13.9% | 0% |
| **INT SACRIFICE 1** | 0/10 (0%) | 0/10 (0%) | 0/10 (0%) |
| **TERMINAL (d)** | 0/1 (0%) | 0/1 (0%) | 0/0 (0%) |
| **FIRST INCIDENCE** | --- | 603 | --- |
| **HC TUMORS SAME ROUTE** | 4/100 (4%) | | |
| **HC TUMORS ALL ROUTES** | 91/1551 (6%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | (n) | (n) | (n) |
| **POLY 1.5** | (n) | (n) | (n) |
| **POLY 6** | (n) | (n) | (n) |
| **COCH-ARM / FISHERS** | (n) | (n) | (n) |
| **MAX-ISO-POLY-3** | (n) | (n) | (n) |
| **HISTCONT SAME RTE** | (n) | (n) | (n) |
| **HISTCONT ALL RTES** | (n) | (n) | (n) |
| **CURR VS HC SAME RTE** | (n) | | |
| **CURR VS HC ALL RTES** | (n) | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 105 WEEKS

| | FEMALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **Lung** | | | |
| **Alveolar/Bronchiolar Carcinoma or Alveolar/Bronchiolar Adenoma** | | | |
| **TUMOR RATES** | | | |
| **OVERALL(a)** | 0/19 (0%) | 1/13 (8%) | 0/17 (0%) |
| **POLY-3 RATE (b)** | 0/9.37 | 1/7.18 | 0/8.78 |
| **POLY-3 PERCENT (g)** | 0% | 13.9% | 0% |
| **INT SACRIFICE 1** | 0/10 (0%) | 0/10 (0%) | 0/10 (0%) |
| **TERMINAL (d)** | 0/1 (0%) | 0/1 (0%) | 0/0 (0%) |
| **FIRST INCIDENCE** | --- | 603 | --- |
| **HC TUMORS SAME ROUTE** | 6/100 (6%) | | |
| **HC TUMORS ALL ROUTES** | 128/1551 (8%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | (n) | (n) | (n) |
| **POLY 1.5** | (n) | (n) | (n) |
| **POLY 6** | (n) | (n) | (n) |
| **COCH-ARM / FISHERS** | (n) | (n) | (n) |
| **MAX-ISO-POLY-3** | (n) | (n) | (n) |
| **HISTCONT SAME RTE** | (n) | (n) | (n) |
| **HISTCONT ALL RTES** | (n) | (n) | (n) |
| **CURR VS HC SAME RTE** | (n) | | |
| **CURR VS HC ALL RTES** | (n) | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 105 WEEKS

| | FEMALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **Pituitary Gland: Pars Distalis or Unspecified Site** | | | |
| **Adenoma** | | | |
| **TUMOR RATES** | # | # | # |
| **OVERALL(a)** | 0/17 (0%) | 2/12 (17%) | 1/17 (6%) |
| **POLY-3 RATE (b)** | 0/8.91 | 2/6.83 | 1/8.80 |
| **POLY-3 PERCENT (g)** | 0% | 29.3% | 11.4% |
| **INT SACRIFICE 1** | 0/9 (0%) | 0/10 (0%) | 0/9 (0%) |
| **TERMINAL (d)** | 0/1 (0%) | 1/1 (100%) | 0/0 (0%) |
| **FIRST INCIDENCE** | --- | 587 | 608 |
| **HC TUMORS SAME ROUTE** | 10/93 (11%) | | |
| **HC TUMORS ALL ROUTES** | 220/1491 (15%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | P=0.314 | P=0.155 | P=0.498 |
| **POLY 1.5** | P=0.341 | P=0.164 | P=0.509 |
| **POLY 6** | P=0.260 | P=0.139 | P=0.473 |
| **COCH-ARM / FISHERS** | P=0.328 | P=0.163 | P=0.500 |
| **MAX-ISO-POLY-3** | P=0.149 | P=0.041* | P=0.153 |
| **HISTCONT SAME RTE** | P=0.423 | P=0.305 | P=1.000 |
| **HISTCONT ALL RTES** | P=0.630 | P=0.418 | P=1.000 |
| **CURR VS HC SAME RTE** | P=0.422 | | |
| **CURR VS HC ALL RTES** | P=0.380 | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 105 WEEKS

| | FEMALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **Uterus** | | | |
| **Sarcoma Stromal** | | | |
| **TUMOR RATES** | # | # | # |
| **OVERALL(a)** | 0/19 (0%) | 2/13 (15%) | 0/17 (0%) |
| **POLY-3 RATE (b)** | 0/9.37 | 2/7.26 | 0/8.78 |
| **POLY-3 PERCENT (g)** | 0% | 27.5% | 0% |
| **INT SACRIFICE 1** | 0/10 (0%) | 0/10 (0%) | 0/10 (0%) |
| **TERMINAL (d)** | 0/1 (0%) | 1/1 (100%) | 0/0 (0%) |
| **FIRST INCIDENCE** | --- | 587 | --- |
| **HC TUMORS SAME ROUTE** | 1/100 (1%) | | |
| **HC TUMORS ALL ROUTES** | 10/1559 (1%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | P=0.597 | P=0.158 | (e) |
| **POLY 1.5** | P=0.613 | P=0.165 | (e) |
| **POLY 6** | P=0.554 | P=0.142 | (e) |
| **COCH-ARM / FISHERS** | P=0.574 | P=0.157 | (e) |
| **MAX-ISO-POLY-3** | P=0.218 | P=0.041* | (e) |
| **HISTCONT SAME RTE** | P=0.419 | P=0.242 | (e) |
| **HISTCONT ALL RTES** | P=0.069 | P=0.006** | (e) |
| **CURR VS HC SAME RTE** | P=0.633 | | |
| **CURR VS HC ALL RTES** | P=0.996 | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 105 WEEKS

| | FEMALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **Uterus** | | | |
| **Sarcoma Stromal or Polyp Stromal** | | | |
| **TUMOR RATES** | # | # | # |
| **OVERALL(a)** | 0/19 (0%) | 2/13 (15%) | 1/17 (6%) |
| **POLY-3 RATE (b)** | 0/9.37 | 2/7.26 | 1/8.95 |
| **POLY-3 PERCENT (g)** | 0% | 27.5% | 11.2% |
| **INT SACRIFICE 1** | 0/10 (0%) | 0/10 (0%) | 0/10 (0%) |
| **TERMINAL (d)** | 0/1 (0%) | 1/1 (100%) | 0/0 (0%) |
| **FIRST INCIDENCE** | --- | 587 | 576 |
| **HC TUMORS SAME ROUTE** | 5/100 (5%) | | |
| **HC TUMORS ALL ROUTES** | 51/1559 (3%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | P=0.313 | P=0.158 | P=0.491 |
| **POLY 1.5** | P=0.329 | P=0.165 | P=0.497 |
| **POLY 6** | P=0.279 | P=0.142 | P=0.477 |
| **COCH-ARM / FISHERS** | P=0.299 | P=0.157 | P=0.472 |
| **MAX-ISO-POLY-3** | P=0.150 | P=0.041* | P=0.149 |
| **HISTCONT SAME RTE** | P=0.325 | P=0.285 | P=1.000 |
| **HISTCONT ALL RTES** | P=0.069 | P=0.101 | P=0.413 |
| **CURR VS HC SAME RTE** | P=0.677 | | |
| **CURR VS HC ALL RTES** | P=0.899 | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 105 WEEKS

| | FEMALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **All Organs** | | | |
| **Benign Tumors** | | | |
| **TUMOR RATES** | # | # | # |
| **OVERALL(a)** | 3/19 (16%) | 5/13 (38%) | 9/17 (53%) |
| **POLY-3 RATE (b)** | 3/10.49 | 5/8.44 | 9/12.41 |
| **POLY-3 PERCENT (g)** | 28.6% | 59.2% | 72.5% |
| **INT SACRIFICE 1** | 1/10 (10%) | 5/10 (50%) | 2/10 (20%) |
| **TERMINAL (d)** | 0/1 (0%) | 1/1 (100%) | 0/0 (0%) |
| **FIRST INCIDENCE** | 462(I) | 462(I) | 455 |
| **HC TUMORS SAME ROUTE** | 54/100 (54%) | | |
| **HC TUMORS ALL ROUTES** | 788/1559 (51%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | P=0.014* | P=0.165 | P=0.024* |
| **POLY 1.5** | P=0.020* | P=0.184 | P=0.027* |
| **POLY 6** | P=0.007** | P=0.125 | P=0.020* |
| **COCH-ARM / FISHERS** | P=0.016* | P=0.150 | P=0.022* |
| **MAX-ISO-POLY-3** | P=0.017* | P=0.070 | P=0.013* |
| **HISTCONT SAME RTE** | P=0.463 | P=1.000 | P=0.392 |
| **HISTCONT ALL RTES** | P=0.296 | P=0.500 | P=0.279 |
| **CURR VS HC SAME RTE** | P=0.236 | | |
| **CURR VS HC ALL RTES** | P=0.213 | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 105 WEEKS

| | FEMALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **All Organs** | | | |
| **Malignant Tumors** | | | |
| **TUMOR RATES** | # | # | # |
| **OVERALL(a)** | 3/19 (16%) | 2/13 (15%) | 4/17 (24%) |
| **POLY-3 RATE (b)** | 3/9.70 | 2/7.26 | 4/10.54 |
| **POLY-3 PERCENT (g)** | 30.9% | 27.5% | 38% |
| **INT SACRIFICE 1** | 0/10 (0%) | 0/10 (0%) | 0/10 (0%) |
| **TERMINAL (d)** | 1/1 (100%) | 1/1 (100%) | 0/0 (0%) |
| **FIRST INCIDENCE** | 543 | 587 | 455 |
| **HC TUMORS SAME ROUTE** | 28/100 (28%) | | |
| **HC TUMORS ALL ROUTES** | 621/1559 (40%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | P=0.474 | P=0.658N | P=0.557 |
| **POLY 1.5** | P=0.457 | P=0.636N | P=0.528 |
| **POLY 6** | P=0.516 | P=0.720N | P=0.622 |
| **COCH-ARM / FISHERS** | P=0.384 | P=0.692 | P=0.434 |
| **MAX-ISO-POLY-3** | P=0.477 | P=0.440N | P=0.372 |
| **HISTCONT SAME RTE** | P=0.387 | P=1.000 | P=0.417 |
| **HISTCONT ALL RTES** | (h) | (h) | (h) |
| **CURR VS HC SAME RTE** | P=0.943 | | |
| **CURR VS HC ALL RTES** | P=0.620 | | |

## STATISTICAL ANALYSIS OF PRIMARY TUMORS IN MOUSE(B6C3F1)
## LAST REMOVAL AT 105 WEEKS

| | FEMALE | | |
|---|---|---|---|
| **DOSE** | **0 MG/KG** | **6.0 MG/K** | **10.0 MG/KG** |
| **All Organs** | | | |
| **Malignant and Benign Tumors** | | | |
| **TUMOR RATES** | # | # | # |
| **OVERALL(a)** | 6/19 (32%) | 5/13 (38%) | 11/17 (65%) |
| **POLY-3 RATE (b)** | 6/10.83 | 5/8.44 | 11/13.42 |
| **POLY-3 PERCENT (g)** | 55.4% | 59.2% | 82% |
| **INT SACRIFICE 1** | 1/10 (10%) | 5/10 (50%) | 2/10 (20%) |
| **TERMINAL (d)** | 1/1 (100%) | 1/1 (100%) | 0/0 (0%) |
| **FIRST INCIDENCE** | 462(I) | 462(I) | 455 |
| **HC TUMORS SAME ROUTE** | 68/100 (68%) | | |
| **HC TUMORS ALL ROUTES** | 1111/1559 (71%) | | |
| **STATISTICAL TESTS** | | | |
| **POLY 3** | P=0.071 | P=0.635 | P=0.111 |
| **POLY 1.5** | P=0.072 | P=0.612 | P=0.094 |
| **POLY 6** | P=0.072 | P=0.661 | P=0.167 |
| **COCH-ARM / FISHERS** | P=0.044* | P=0.487 | P=0.049* |
| **MAX-ISO-POLY-3** | P=0.086 | P=0.425 | P=0.057 |
| **HISTCONT SAME RTE** | P=0.415 | P=1.000 | P=0.384 |
| **HISTCONT ALL RTES** | P=0.518 | P=1.000 | P=0.414 |
| **CURR VS HC SAME RTE** | P=0.406 | | |
| **CURR VS HC ALL RTES** | P=0.278 | | |

**LEGEND**

| | |
|---|---|
| (a) | Number of tumor-bearing animals/number of animals examined at site. |
| (b) | Number of tumor-bearing animals/Poly-3 number |
| (d) | Observed incidence at terminal kill. |
| (e) | Value of statistic cannot be computed. |
| (f) | Beneath the control incidence are the P-values associated with the trend test. Beneath the dosed group incidence are the P-values corresponding to pairwise comparisons between the controls and that dosed group. |
| (g) | Poly-3 adjusted lifetime tumor incidence. |
| (n) | No statistics are calculated if all dose groups have fewer than two tumors. |
| (I) | Interim sacrifice |
| (T) | Terminal sacrifice |
| # | Tumor rates based on numbers of animals necropsied. |
| * | To the right of any statistical result, indicates significance at (P<=0.05). |
| ** | To the right of any statistical result, indicates significance at (P<=0.01). |
| N | Indicates a negative trend for all tests |
| | The Cochran-Armitage and Fishers exact tests compare directly the overall incidence rates. |

** END OF REPORT **