

TDMS No. 20516 - 02

Test Type: 90-DAY

Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

P10: STATISTICAL ANALYSIS OF NON-NEOPLASTIC LESIONS

Metal working fluids (Trim SC210)

CAS Number: TRIMSC210

Date Report Requested: 08/25/2008

Time Report Requested: 10:20:23

First Dose M/F: 08/14/06 / 08/14/06

Lab: BNW

F1_M3

C Number: C20516
Lock Date: 05/16/2007
Cage Range: ALL
Date Range: ALL
Reasons For Removal: ALL
Removal Date Range: ALL
Treatment Groups: Include ALL
Study Gender: Both
TDMSE Version: 2.0.0

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SUMMARY OF STATISTICALLY SIGNIFICANT (P<=.05) RESULTS IN THE ANALYSIS OF Metal working fluids (Trim SC210)

MALE MICE

Organ

Larynx

Larynx: Squamous Epithelium

Lung

Lung: Bronchiole

Lung: Perivascular

Nose: Olfactory Epithelium

Nose: Respiratory Epithelium

Morphology

Inflammation Chronic

Metaplasia

Hyperplasia

Infiltration Cellular Histiocyte

Hyperplasia

Inflammation Chronic

Accumulation, Hyaline Droplet

Accumulation, Hyaline Droplet

FEMALE MICE

Organ

Larynx

Larynx: Squamous Epithelium

Lung

Lung: Bronchiole

Lung: Perivascular

Nose: Olfactory Epithelium

Nose: Respiratory Epithelium

Morphology

Inflammation Chronic

Metaplasia

Hyperplasia

Infiltration Cellular Histiocyte

Hyperplasia

Inflammation Chronic

Accumulation, Hyaline Droplet

Accumulation, Hyaline Droplet

**STATISTICAL ANALYSIS OF NON-NEOPLASTIC LESIONS IN MICE(B6C3F1)
TERMINAL SACRIFICE AT 14 WEEKS**

| DOSE | Males | | | | | |
|------|---------|----------|----------|-----------|-----------|-----------|
| | 0 mg/m3 | 25 mg/m3 | 50 mg/m3 | 100 mg/m3 | 200 mg/m3 | 400 mg/m3 |

**Kidney
Nephropathy**

LESION RATES

| | | | | | | |
|--------------------|------------|----------|----------|----------|----------|-----------|
| OVERALL (a) | 2/10 (20%) | 0/0 (0%) | 0/0 (0%) | 0/0 (0%) | 0/0 (0%) | 0/10 (0%) |
| POLY-3 RATE (b) | 2/10.00 | 0/0.00 | 0/0.00 | 0/0.00 | 0/0.00 | 0/10.00 |
| POLY-3 PERCENT (g) | 20% | 0% | 0% | 0% | 0% | 0% |
| TERMINAL (d) | 2/10 (20%) | 0/0 (0%) | 0/0 (0%) | 0/0 (0%) | 0/0 (0%) | 0/10 (0%) |
| FIRST INCIDENCE | 95 (T) | --- | --- | --- | --- | --- |

STATISTICAL TESTS

| | | | | | | |
|--------------------|----------|-----|-----|-----|-----|----------|
| POLY 3 | (e) | (e) | (e) | (e) | (e) | P=0.227N |
| POLY 1.5 | (e) | (e) | (e) | (e) | (e) | P=0.227N |
| POLY 6 | (e) | (e) | (e) | (e) | (e) | P=0.227N |
| COCH-ARM / FISHERS | P=0.132N | (e) | (e) | (e) | (e) | P=0.237N |
| MAX-ISO-POLY-3 | (e) | (e) | (e) | (e) | (e) | P=0.066N |

**STATISTICAL ANALYSIS OF NON-NEOPLASTIC LESIONS IN MICE(B6C3F1)
TERMINAL SACRIFICE AT 14 WEEKS**

| DOSE | Males | | | | | |
|------|---------|----------|----------|-----------|-----------|-----------|
| | 0 mg/m3 | 25 mg/m3 | 50 mg/m3 | 100 mg/m3 | 200 mg/m3 | 400 mg/m3 |

**Larynx
Inflammation Chronic**

LESION RATES

| | | | | | | |
|--------------------|-----------|-----------|-----------|------------|------------|------------|
| OVERALL (a) | 0/10 (0%) | 0/10 (0%) | 0/10 (0%) | 2/10 (20%) | 3/10 (30%) | 1/10 (10%) |
| POLY-3 RATE (b) | 0/10.00 | 0/10.00 | 0/10.00 | 2/10.00 | 3/10.00 | 1/10.00 |
| POLY-3 PERCENT (g) | 0% | 0% | 0% | 20% | 30% | 10% |
| TERMINAL (d) | 0/10 (0%) | 0/10 (0%) | 0/10 (0%) | 2/10 (20%) | 3/10 (30%) | 1/10 (10%) |
| FIRST INCIDENCE | --- | --- | --- | 95 (T) | 95 (T) | 95 (T) |

STATISTICAL TESTS

| | | | | | | |
|--------------------|---------|-----|-----|---------|----------|---------|
| POLY 3 | P=0.147 | (e) | (e) | P=0.227 | P=0.095 | P=0.500 |
| POLY 1.5 | P=0.147 | (e) | (e) | P=0.227 | P=0.095 | P=0.500 |
| POLY 6 | P=0.147 | (e) | (e) | P=0.227 | P=0.095 | P=0.500 |
| COCH-ARM / FISHERS | P=0.154 | (e) | (e) | P=0.237 | P=0.105 | P=0.500 |
| MAX-ISO-POLY-3 | P=0.062 | (e) | (e) | P=0.066 | P=0.025* | P=0.158 |

**STATISTICAL ANALYSIS OF NON-NEOPLASTIC LESIONS IN MICE(B6C3F1)
TERMINAL SACRIFICE AT 14 WEEKS**

| DOSE | Males | | | | | |
|------|---------|----------|----------|-----------|-----------|-----------|
| | 0 mg/m3 | 25 mg/m3 | 50 mg/m3 | 100 mg/m3 | 200 mg/m3 | 400 mg/m3 |

**Larynx
Metaplasia**

LESION RATES

| | | | | | | |
|--------------------|-----------|--------------|--------------|--------------|--------------|--------------|
| OVERALL (a) | 0/10 (0%) | 10/10 (100%) | 10/10 (100%) | 10/10 (100%) | 10/10 (100%) | 10/10 (100%) |
| POLY-3 RATE (b) | 0/10.00 | 10/10.00 | 10/10.00 | 10/10.00 | 10/10.00 | 10/10.00 |
| POLY-3 PERCENT (g) | 0% | 100% | 100% | 100% | 100% | 100% |
| TERMINAL (d) | 0/10 (0%) | 10/10 (100%) | 10/10 (100%) | 10/10 (100%) | 10/10 (100%) | 10/10 (100%) |
| FIRST INCIDENCE | --- | 95 (T) | 95 (T) | 95 (T) | 95 (T) | 95 (T) |

STATISTICAL TESTS

| | | | | | | |
|--------------------|-----------|-----------|-----------|-----------|-----------|-----------|
| POLY 3 | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** |
| POLY 1.5 | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** |
| POLY 6 | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** |
| COCH-ARM / FISHERS | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** |
| MAX-ISO-POLY-3 | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** |

**STATISTICAL ANALYSIS OF NON-NEOPLASTIC LESIONS IN MICE(B6C3F1)
TERMINAL SACRIFICE AT 14 WEEKS**

| DOSE | Males | | | | | |
|------|---------|----------|----------|-----------|-----------|-----------|
| | 0 mg/m3 | 25 mg/m3 | 50 mg/m3 | 100 mg/m3 | 200 mg/m3 | 400 mg/m3 |

**Larynx: Squamous Epithelium
Hyperplasia**

LESION RATES

| | | | | | | |
|--------------------|-----------|-----------|-----------|------------|--------------|------------|
| OVERALL (a) | 0/10 (0%) | 0/10 (0%) | 0/10 (0%) | 6/10 (60%) | 10/10 (100%) | 9/10 (90%) |
| POLY-3 RATE (b) | 0/10.00 | 0/10.00 | 0/10.00 | 6/10.00 | 10/10.00 | 9/10.00 |
| POLY-3 PERCENT (g) | 0% | 0% | 0% | 60% | 100% | 90% |
| TERMINAL (d) | 0/10 (0%) | 0/10 (0%) | 0/10 (0%) | 6/10 (60%) | 10/10 (100%) | 9/10 (90%) |
| FIRST INCIDENCE | --- | --- | --- | 95 (T) | 95 (T) | 95 (T) |

STATISTICAL TESTS

| | | | | | | |
|--------------------|-----------|-----|-----|-----------|-----------|-----------|
| POLY 3 | P<0.001** | (e) | (e) | P<0.001** | P<0.001** | P<0.001** |
| POLY 1.5 | P<0.001** | (e) | (e) | P<0.001** | P<0.001** | P<0.001** |
| POLY 6 | P<0.001** | (e) | (e) | P<0.001** | P<0.001** | P<0.001** |
| COCH-ARM / FISHERS | P<0.001** | (e) | (e) | P=0.005** | P<0.001** | P<0.001** |
| MAX-ISO-POLY-3 | P<0.001** | (e) | (e) | P<0.001** | P<0.001** | P<0.001** |

**STATISTICAL ANALYSIS OF NON-NEOPLASTIC LESIONS IN MICE(B6C3F1)
TERMINAL SACRIFICE AT 14 WEEKS**

| DOSE | Males | | | | | |
|------|---------|----------|----------|-----------|-----------|-----------|
| | 0 mg/m3 | 25 mg/m3 | 50 mg/m3 | 100 mg/m3 | 200 mg/m3 | 400 mg/m3 |

**Lung
Infiltration Cellular Histiocyte**

LESION RATES

| | | | | | | |
|--------------------|-----------|-----------|-----------|------------|--------------|--------------|
| OVERALL (a) | 0/10 (0%) | 0/10 (0%) | 0/10 (0%) | 1/10 (10%) | 10/10 (100%) | 10/10 (100%) |
| POLY-3 RATE (b) | 0/10.00 | 0/10.00 | 0/10.00 | 1/10.00 | 10/10.00 | 10/10.00 |
| POLY-3 PERCENT (g) | 0% | 0% | 0% | 10% | 100% | 100% |
| TERMINAL (d) | 0/10 (0%) | 0/10 (0%) | 0/10 (0%) | 1/10 (10%) | 10/10 (100%) | 10/10 (100%) |
| FIRST INCIDENCE | --- | --- | --- | 95 (T) | 95 (T) | 95 (T) |

STATISTICAL TESTS

| | | | | | | |
|--------------------|-----------|-----|-----|---------|-----------|-----------|
| POLY 3 | P<0.001** | (e) | (e) | P=0.500 | P<0.001** | P<0.001** |
| POLY 1.5 | P<0.001** | (e) | (e) | P=0.500 | P<0.001** | P<0.001** |
| POLY 6 | P<0.001** | (e) | (e) | P=0.500 | P<0.001** | P<0.001** |
| COCH-ARM / FISHERS | P<0.001** | (e) | (e) | P=0.500 | P<0.001** | P<0.001** |
| MAX-ISO-POLY-3 | P<0.001** | (e) | (e) | P=0.158 | P<0.001** | P<0.001** |

**STATISTICAL ANALYSIS OF NON-NEOPLASTIC LESIONS IN MICE(B6C3F1)
TERMINAL SACRIFICE AT 14 WEEKS**

| DOSE | Males | | | | | |
|------|---------|----------|----------|-----------|-----------|-----------|
| | 0 mg/m3 | 25 mg/m3 | 50 mg/m3 | 100 mg/m3 | 200 mg/m3 | 400 mg/m3 |

**Lung: Bronchiole
Hyperplasia**

LESION RATES

| | | | | | | |
|--------------------|-----------|-----------|-----------|-----------|--------------|--------------|
| OVERALL (a) | 0/10 (0%) | 0/10 (0%) | 0/10 (0%) | 0/10 (0%) | 10/10 (100%) | 10/10 (100%) |
| POLY-3 RATE (b) | 0/10.00 | 0/10.00 | 0/10.00 | 0/10.00 | 10/10.00 | 10/10.00 |
| POLY-3 PERCENT (g) | 0% | 0% | 0% | 0% | 100% | 100% |
| TERMINAL (d) | 0/10 (0%) | 0/10 (0%) | 0/10 (0%) | 0/10 (0%) | 10/10 (100%) | 10/10 (100%) |
| FIRST INCIDENCE | --- | --- | --- | --- | 95 (T) | 95 (T) |

STATISTICAL TESTS

| | | | | | | |
|--------------------|-----------|-----|-----|-----|-----------|-----------|
| POLY 3 | P<0.001** | (e) | (e) | (e) | P<0.001** | P<0.001** |
| POLY 1.5 | P<0.001** | (e) | (e) | (e) | P<0.001** | P<0.001** |
| POLY 6 | P<0.001** | (e) | (e) | (e) | P<0.001** | P<0.001** |
| COCH-ARM / FISHERS | P<0.001** | (e) | (e) | (e) | P<0.001** | P<0.001** |
| MAX-ISO-POLY-3 | P<0.001** | (e) | (e) | (e) | P<0.001** | P<0.001** |

**STATISTICAL ANALYSIS OF NON-NEOPLASTIC LESIONS IN MICE(B6C3F1)
TERMINAL SACRIFICE AT 14 WEEKS**

| DOSE | Males | | | | | |
|------|---------|----------|----------|-----------|-----------|-----------|
| | 0 mg/m3 | 25 mg/m3 | 50 mg/m3 | 100 mg/m3 | 200 mg/m3 | 400 mg/m3 |

**Lung: Perivascular
Inflammation Chronic**

LESION RATES

| | | | | | | |
|--------------------|-----------|------------|-----------|------------|--------------|--------------|
| OVERALL (a) | 0/10 (0%) | 1/10 (10%) | 0/10 (0%) | 2/10 (20%) | 10/10 (100%) | 10/10 (100%) |
| POLY-3 RATE (b) | 0/10.00 | 1/10.00 | 0/10.00 | 2/10.00 | 10/10.00 | 10/10.00 |
| POLY-3 PERCENT (g) | 0% | 10% | 0% | 20% | 100% | 100% |
| TERMINAL (d) | 0/10 (0%) | 1/10 (10%) | 0/10 (0%) | 2/10 (20%) | 10/10 (100%) | 10/10 (100%) |
| FIRST INCIDENCE | --- | 95 (T) | --- | 95 (T) | 95 (T) | 95 (T) |

STATISTICAL TESTS

| | | | | | | |
|--------------------|-----------|---------|-----|---------|-----------|-----------|
| POLY 3 | P<0.001** | P=0.500 | (e) | P=0.227 | P<0.001** | P<0.001** |
| POLY 1.5 | P<0.001** | P=0.500 | (e) | P=0.227 | P<0.001** | P<0.001** |
| POLY 6 | P<0.001** | P=0.500 | (e) | P=0.227 | P<0.001** | P<0.001** |
| COCH-ARM / FISHERS | P<0.001** | P=0.500 | (e) | P=0.237 | P<0.001** | P<0.001** |
| MAX-ISO-POLY-3 | P<0.001** | P=0.158 | (e) | P=0.066 | P<0.001** | P<0.001** |

**STATISTICAL ANALYSIS OF NON-NEOPLASTIC LESIONS IN MICE(B6C3F1)
TERMINAL SACRIFICE AT 14 WEEKS**

| DOSE | Males | | | | | |
|------|---------|----------|----------|-----------|-----------|-----------|
| | 0 mg/m3 | 25 mg/m3 | 50 mg/m3 | 100 mg/m3 | 200 mg/m3 | 400 mg/m3 |

**Nose: Olfactory Epithelium
Accumulation, Hyaline Droplet**

LESION RATES

| | | | | | | |
|--------------------|-----------|------------|------------|------------|--------------|--------------|
| OVERALL (a) | 0/10 (0%) | 1/10 (10%) | 2/10 (20%) | 7/10 (70%) | 10/10 (100%) | 10/10 (100%) |
| POLY-3 RATE (b) | 0/10.00 | 1/10.00 | 2/10.00 | 7/10.00 | 10/10.00 | 10/10.00 |
| POLY-3 PERCENT (g) | 0% | 10% | 20% | 70% | 100% | 100% |
| TERMINAL (d) | 0/10 (0%) | 1/10 (10%) | 2/10 (20%) | 7/10 (70%) | 10/10 (100%) | 10/10 (100%) |
| FIRST INCIDENCE | --- | 95 (T) | 95 (T) | 95 (T) | 95 (T) | 95 (T) |

STATISTICAL TESTS

| | | | | | | |
|--------------------|-----------|---------|---------|-----------|-----------|-----------|
| POLY 3 | P<0.001** | P=0.500 | P=0.227 | P<0.001** | P<0.001** | P<0.001** |
| POLY 1.5 | P<0.001** | P=0.500 | P=0.227 | P<0.001** | P<0.001** | P<0.001** |
| POLY 6 | P<0.001** | P=0.500 | P=0.227 | P<0.001** | P<0.001** | P<0.001** |
| COCH-ARM / FISHERS | P<0.001** | P=0.500 | P=0.237 | P=0.002** | P<0.001** | P<0.001** |
| MAX-ISO-POLY-3 | P<0.001** | P=0.158 | P=0.066 | P<0.001** | P<0.001** | P<0.001** |

**STATISTICAL ANALYSIS OF NON-NEOPLASTIC LESIONS IN MICE(B6C3F1)
TERMINAL SACRIFICE AT 14 WEEKS**

| DOSE | Males | | | | | |
|------|---------|----------|----------|-----------|-----------|-----------|
| | 0 mg/m3 | 25 mg/m3 | 50 mg/m3 | 100 mg/m3 | 200 mg/m3 | 400 mg/m3 |

**Nose: Respiratory Epithelium
Accumulation, Hyaline Droplet**

LESION RATES

| | | | | | | |
|--------------------|-----------|------------|--------------|--------------|--------------|--------------|
| OVERALL (a) | 0/10 (0%) | 9/10 (90%) | 10/10 (100%) | 10/10 (100%) | 10/10 (100%) | 10/10 (100%) |
| POLY-3 RATE (b) | 0/10.00 | 9/10.00 | 10/10.00 | 10/10.00 | 10/10.00 | 10/10.00 |
| POLY-3 PERCENT (g) | 0% | 90% | 100% | 100% | 100% | 100% |
| TERMINAL (d) | 0/10 (0%) | 9/10 (90%) | 10/10 (100%) | 10/10 (100%) | 10/10 (100%) | 10/10 (100%) |
| FIRST INCIDENCE | --- | 95 (T) | 95 (T) | 95 (T) | 95 (T) | 95 (T) |

STATISTICAL TESTS

| | | | | | | |
|--------------------|-----------|-----------|-----------|-----------|-----------|-----------|
| POLY 3 | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** |
| POLY 1.5 | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** |
| POLY 6 | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** |
| COCH-ARM / FISHERS | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** |
| MAX-ISO-POLY-3 | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** |

**STATISTICAL ANALYSIS OF NON-NEOPLASTIC LESIONS IN MICE(B6C3F1)
TERMINAL SACRIFICE AT 14 WEEKS**

| DOSE | Females | | | | |
|------|---------|----------|-----------|-----------|-----------|
| | 0 mg/m3 | 50 mg/m3 | 100 mg/m3 | 200 mg/m3 | 400 mg/m3 |

**Kidney
Nephropathy**

LESION RATES

| | | | | | |
|--------------------|------------|----------|----------|----------|------------|
| OVERALL (a) | 1/10 (10%) | 0/0 (0%) | 0/0 (0%) | 0/0 (0%) | 1/10 (10%) |
| POLY-3 RATE (b) | 1/10.00 | 0/0.00 | 0/0.00 | 0/0.00 | 1/10.00 |
| POLY-3 PERCENT (g) | 10% | 0% | 0% | 0% | 10% |
| TERMINAL (d) | 1/10 (10%) | 0/0 (0%) | 0/0 (0%) | 0/0 (0%) | 1/10 (10%) |
| FIRST INCIDENCE | 96 (T) | --- | --- | --- | 96 (T) |

STATISTICAL TESTS

| | | | | | |
|--------------------|---------|-----|-----|-----|----------|
| POLY 3 | (e) | (e) | (e) | (e) | P=0.760 |
| POLY 1.5 | (e) | (e) | (e) | (e) | P=0.760 |
| POLY 6 | (e) | (e) | (e) | (e) | P=0.760 |
| COCH-ARM / FISHERS | P=0.645 | (e) | (e) | (e) | P=0.763N |
| MAX-ISO-POLY-3 | (e) | (e) | (e) | (e) | P=1.000 |

**STATISTICAL ANALYSIS OF NON-NEOPLASTIC LESIONS IN MICE(B6C3F1)
TERMINAL SACRIFICE AT 14 WEEKS**

| DOSE | Females | | | | |
|------|---------|----------|-----------|-----------|-----------|
| | 0 mg/m3 | 50 mg/m3 | 100 mg/m3 | 200 mg/m3 | 400 mg/m3 |

**Larynx
Inflammation Chronic**

LESION RATES

| | | | | | |
|--------------------|-----------|-----------|-----------|----------|------------|
| OVERALL (a) | 0/10 (0%) | 0/20 (0%) | 0/10 (0%) | 0/9 (0%) | 1/10 (10%) |
| POLY-3 RATE (b) | 0/10.00 | 0/20.00 | 0/10.00 | 0/9.00 | 1/10.00 |
| POLY-3 PERCENT (g) | 0% | 0% | 0% | 0% | 10% |
| TERMINAL (d) | 0/10 (0%) | 0/20 (0%) | 0/10 (0%) | 0/9 (0%) | 1/10 (10%) |
| FIRST INCIDENCE | --- | --- | --- | --- | 96 (T) |

STATISTICAL TESTS

| | | | | | |
|--------------------|----------|-----|-----|-----|---------|
| POLY 3 | P=0.105 | (e) | (e) | (e) | P=0.500 |
| POLY 1.5 | P=0.105 | (e) | (e) | (e) | P=0.500 |
| POLY 6 | P=0.105 | (e) | (e) | (e) | P=0.500 |
| COCH-ARM / FISHERS | P=0.105 | (e) | (e) | (e) | P=0.500 |
| MAX-ISO-POLY-3 | P=0.041* | (e) | (e) | (e) | P=0.158 |

**STATISTICAL ANALYSIS OF NON-NEOPLASTIC LESIONS IN MICE(B6C3F1)
TERMINAL SACRIFICE AT 14 WEEKS**

| DOSE | Females | | | | |
|------|---------|----------|-----------|-----------|-----------|
| | 0 mg/m3 | 50 mg/m3 | 100 mg/m3 | 200 mg/m3 | 400 mg/m3 |

**Larynx
Metaplasia**

LESION RATES

| | | | | | |
|--------------------|-----------|--------------|--------------|------------|--------------|
| OVERALL (a) | 0/10 (0%) | 20/20 (100%) | 10/10 (100%) | 9/9 (100%) | 10/10 (100%) |
| POLY-3 RATE (b) | 0/10.00 | 20/20.00 | 10/10.00 | 9/9.00 | 10/10.00 |
| POLY-3 PERCENT (g) | 0% | 100% | 100% | 100% | 100% |
| TERMINAL (d) | 0/10 (0%) | 20/20 (100%) | 10/10 (100%) | 9/9 (100%) | 10/10 (100%) |
| FIRST INCIDENCE | --- | 96 (T) | 96 (T) | 96 (T) | 96 (T) |

STATISTICAL TESTS

| | | | | | |
|--------------------|-----------|-----------|-----------|-----------|-----------|
| POLY 3 | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** |
| POLY 1.5 | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** |
| POLY 6 | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** |
| COCH-ARM / FISHERS | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** |
| MAX-ISO-POLY-3 | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** |

**STATISTICAL ANALYSIS OF NON-NEOPLASTIC LESIONS IN MICE(B6C3F1)
TERMINAL SACRIFICE AT 14 WEEKS**

| DOSE | Females | | | | |
|------|---------|----------|-----------|-----------|-----------|
| | 0 mg/m3 | 50 mg/m3 | 100 mg/m3 | 200 mg/m3 | 400 mg/m3 |

**Larynx: Squamous Epithelium
Hyperplasia**

LESION RATES

| | | | | | |
|--------------------|-----------|-----------|------------|-----------|------------|
| OVERALL (a) | 0/10 (0%) | 0/20 (0%) | 9/10 (90%) | 8/9 (89%) | 8/10 (80%) |
| POLY-3 RATE (b) | 0/10.00 | 0/20.00 | 9/10.00 | 8/9.00 | 8/10.00 |
| POLY-3 PERCENT (g) | 0% | 0% | 90% | 88.9% | 80% |
| TERMINAL (d) | 0/10 (0%) | 0/20 (0%) | 9/10 (90%) | 8/9 (89%) | 8/10 (80%) |
| FIRST INCIDENCE | --- | --- | 96 (T) | 96 (T) | 96 (T) |

STATISTICAL TESTS

| | | | | | |
|--------------------|-----------|-----|-----------|-----------|-----------|
| POLY 3 | P<0.001** | (e) | P<0.001** | P<0.001** | P<0.001** |
| POLY 1.5 | P<0.001** | (e) | P<0.001** | P<0.001** | P<0.001** |
| POLY 6 | P<0.001** | (e) | P<0.001** | P<0.001** | P<0.001** |
| COCH-ARM / FISHERS | P<0.001** | (e) | P<0.001** | P<0.001** | P<0.001** |
| MAX-ISO-POLY-3 | P<0.001** | (e) | P<0.001** | P<0.001** | P<0.001** |

**STATISTICAL ANALYSIS OF NON-NEOPLASTIC LESIONS IN MICE(B6C3F1)
TERMINAL SACRIFICE AT 14 WEEKS**

| DOSE | Females | | | | |
|------|---------|----------|-----------|-----------|-----------|
| | 0 mg/m3 | 50 mg/m3 | 100 mg/m3 | 200 mg/m3 | 400 mg/m3 |

**Lung
Infiltration Cellular Histiocyte**

LESION RATES

| | | | | | |
|--------------------|-----------|-----------|-----------|------------|--------------|
| OVERALL (a) | 0/10 (0%) | 0/20 (0%) | 0/10 (0%) | 9/10 (90%) | 10/10 (100%) |
| POLY-3 RATE (b) | 0/10.00 | 0/20.00 | 0/10.00 | 9/10.00 | 10/10.00 |
| POLY-3 PERCENT (g) | 0% | 0% | 0% | 90% | 100% |
| TERMINAL (d) | 0/10 (0%) | 0/20 (0%) | 0/10 (0%) | 9/10 (90%) | 10/10 (100%) |
| FIRST INCIDENCE | --- | --- | --- | 96 (T) | 96 (T) |

STATISTICAL TESTS

| | | | | | |
|--------------------|-----------|-----|-----|-----------|-----------|
| POLY 3 | P<0.001** | (e) | (e) | P<0.001** | P<0.001** |
| POLY 1.5 | P<0.001** | (e) | (e) | P<0.001** | P<0.001** |
| POLY 6 | P<0.001** | (e) | (e) | P<0.001** | P<0.001** |
| COCH-ARM / FISHERS | P<0.001** | (e) | (e) | P<0.001** | P<0.001** |
| MAX-ISO-POLY-3 | P<0.001** | (e) | (e) | P<0.001** | P<0.001** |

**STATISTICAL ANALYSIS OF NON-NEOPLASTIC LESIONS IN MICE(B6C3F1)
TERMINAL SACRIFICE AT 14 WEEKS**

| DOSE | Females | | | | |
|------|---------|----------|-----------|-----------|-----------|
| | 0 mg/m3 | 50 mg/m3 | 100 mg/m3 | 200 mg/m3 | 400 mg/m3 |

**Lung: Bronchiole
Hyperplasia**

LESION RATES

| | | | | | |
|--------------------|-----------|-----------|-----------|------------|--------------|
| OVERALL (a) | 0/10 (0%) | 0/20 (0%) | 0/10 (0%) | 2/10 (20%) | 10/10 (100%) |
| POLY-3 RATE (b) | 0/10.00 | 0/20.00 | 0/10.00 | 2/10.00 | 10/10.00 |
| POLY-3 PERCENT (g) | 0% | 0% | 0% | 20% | 100% |
| TERMINAL (d) | 0/10 (0%) | 0/20 (0%) | 0/10 (0%) | 2/10 (20%) | 10/10 (100%) |
| FIRST INCIDENCE | --- | --- | --- | 96 (T) | 96 (T) |

STATISTICAL TESTS

| | | | | | |
|--------------------|-----------|-----|-----|---------|-----------|
| POLY 3 | P<0.001** | (e) | (e) | P=0.227 | P<0.001** |
| POLY 1.5 | P<0.001** | (e) | (e) | P=0.227 | P<0.001** |
| POLY 6 | P<0.001** | (e) | (e) | P=0.227 | P<0.001** |
| COCH-ARM / FISHERS | P<0.001** | (e) | (e) | P=0.237 | P<0.001** |
| MAX-ISO-POLY-3 | P<0.001** | (e) | (e) | P=0.066 | P<0.001** |

**STATISTICAL ANALYSIS OF NON-NEOPLASTIC LESIONS IN MICE(B6C3F1)
TERMINAL SACRIFICE AT 14 WEEKS**

| DOSE | Females | | | | |
|------|---------|----------|-----------|-----------|-----------|
| | 0 mg/m3 | 50 mg/m3 | 100 mg/m3 | 200 mg/m3 | 400 mg/m3 |

**Lung: Perivascular
Inflammation Chronic**

LESION RATES

| | | | | | |
|--------------------|-----------|-----------|-----------|------------|--------------|
| OVERALL (a) | 0/10 (0%) | 1/20 (5%) | 0/10 (0%) | 7/10 (70%) | 10/10 (100%) |
| POLY-3 RATE (b) | 0/10.00 | 1/20.00 | 0/10.00 | 7/10.00 | 10/10.00 |
| POLY-3 PERCENT (g) | 0% | 5% | 0% | 70% | 100% |
| TERMINAL (d) | 0/10 (0%) | 1/20 (5%) | 0/10 (0%) | 7/10 (70%) | 10/10 (100%) |
| FIRST INCIDENCE | --- | 96 (T) | --- | 96 (T) | 96 (T) |

STATISTICAL TESTS

| | | | | | |
|--------------------|-----------|---------|-----|-----------|-----------|
| POLY 3 | P<0.001** | P=0.637 | (e) | P<0.001** | P<0.001** |
| POLY 1.5 | P<0.001** | P=0.637 | (e) | P<0.001** | P<0.001** |
| POLY 6 | P<0.001** | P=0.637 | (e) | P<0.001** | P<0.001** |
| COCH-ARM / FISHERS | P<0.001** | P=0.667 | (e) | P=0.002** | P<0.001** |
| MAX-ISO-POLY-3 | P<0.001** | P=0.272 | (e) | P<0.001** | P<0.001** |

**STATISTICAL ANALYSIS OF NON-NEOPLASTIC LESIONS IN MICE(B6C3F1)
TERMINAL SACRIFICE AT 14 WEEKS**

| DOSE | Females | | | | |
|------|---------|----------|-----------|-----------|-----------|
| | 0 mg/m3 | 50 mg/m3 | 100 mg/m3 | 200 mg/m3 | 400 mg/m3 |

**Nose: Olfactory Epithelium
Accumulation, Hyaline Droplet**

LESION RATES

| | | | | | |
|--------------------|------------|------------|------------|--------------|--------------|
| OVERALL (a) | 1/10 (10%) | 6/20 (30%) | 9/10 (90%) | 10/10 (100%) | 10/10 (100%) |
| POLY-3 RATE (b) | 1/10.00 | 6/20.00 | 9/10.00 | 10/10.00 | 10/10.00 |
| POLY-3 PERCENT (g) | 10% | 30% | 90% | 100% | 100% |
| TERMINAL (d) | 1/10 (10%) | 6/20 (30%) | 9/10 (90%) | 10/10 (100%) | 10/10 (100%) |
| FIRST INCIDENCE | 96 (T) | 96 (T) | 96 (T) | 96 (T) | 96 (T) |

STATISTICAL TESTS

| | | | | | |
|--------------------|-----------|---------|-----------|-----------|-----------|
| POLY 3 | P<0.001** | P=0.225 | P<0.001** | P<0.001** | P<0.001** |
| POLY 1.5 | P<0.001** | P=0.225 | P<0.001** | P<0.001** | P<0.001** |
| POLY 6 | P<0.001** | P=0.225 | P<0.001** | P<0.001** | P<0.001** |
| COCH-ARM / FISHERS | P<0.001** | P=0.228 | P<0.001** | P<0.001** | P<0.001** |
| MAX-ISO-POLY-3 | P<0.001** | P=0.146 | P<0.001** | P<0.001** | P<0.001** |

**STATISTICAL ANALYSIS OF NON-NEOPLASTIC LESIONS IN MICE(B6C3F1)
TERMINAL SACRIFICE AT 14 WEEKS**

| DOSE | Females | | | | |
|------|---------|----------|-----------|-----------|-----------|
| | 0 mg/m3 | 50 mg/m3 | 100 mg/m3 | 200 mg/m3 | 400 mg/m3 |

**Nose: Respiratory Epithelium
Accumulation, Hyaline Droplet**

LESION RATES

| | | | | | |
|--------------------|------------|--------------|--------------|--------------|--------------|
| OVERALL (a) | 1/10 (10%) | 20/20 (100%) | 10/10 (100%) | 10/10 (100%) | 10/10 (100%) |
| POLY-3 RATE (b) | 1/10.00 | 20/20.00 | 10/10.00 | 10/10.00 | 10/10.00 |
| POLY-3 PERCENT (g) | 10% | 100% | 100% | 100% | 100% |
| TERMINAL (d) | 1/10 (10%) | 20/20 (100%) | 10/10 (100%) | 10/10 (100%) | 10/10 (100%) |
| FIRST INCIDENCE | 96 (T) | 96 (T) | 96 (T) | 96 (T) | 96 (T) |

STATISTICAL TESTS

| | | | | | |
|--------------------|-----------|-----------|-----------|-----------|-----------|
| POLY 3 | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** |
| POLY 1.5 | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** |
| POLY 6 | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** |
| COCH-ARM / FISHERS | P=0.002** | P<0.001** | P<0.001** | P<0.001** | P<0.001** |
| MAX-ISO-POLY-3 | P<0.001** | P<0.001** | P<0.001** | P<0.001** | P<0.001** |

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.
 - (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. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death.
 - (e) Value of Statistic cannot be computed.
 - (g) Poly-3 adjusted lifetime tumor incidence.
 - (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
- Logistic regression is an alternative method for analyzing the incidence of non-fatal tumors.
The Cochran-Armitage and Fishers exact tests compare directly the overall incidence rates.

*** END OF REPORT ***