

TDMS No. 88006 - 04

Test Type: CHRONIC

Route: RESPIRATORY EXPOSURE WHOLE BODY

Species/Strain: MICE/B6C3F1

P05: INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)
ALPHA-METHYLSTYRENE

CAS Number: 98-83-9

Pathologist: GRUMBEIN, S.

Final 1 Mice

Date Report Reqsted: 07/28/2005

Time Report Reqsted: 09:53:34

First Dose M/F: 07/30/01 / 07/30/01

Lab: BNW

C Number: C88006B
Lock Date: 03/08/2004
Cage Range: ALL
Date Range: ALL
Reasons For Removal: ALL
Removal Date Range: ALL
Treatment Groups: Include ALL

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Lab: BNW

| B6C3F1 MICE MALE | CONTROL | 100 PPM | 300 PPM | 600 PPM |
|---------------------------------------|----------|----------|----------|----------|
| Disposition Summary | | | | |
| Animals Initially in Study | 50 | 50 | 50 | 50 |
| Early Deaths | | | | |
| Moribund Sacrifice | 5 | 8 | 7 | 9 |
| Natural Death | 10 | 10 | 3 | 5 |
| Survivors | | | | |
| Terminal Sacrifice | 35 | 32 | 40 | 36 |
| Animals Examined Microscopically | 50 | 50 | 50 | 50 |
| ALIMENTARY SYSTEM | | | | |
| Intestine Large, Cecum | (43) | (42) | (47) | (45) |
| Intestine Large, Colon | (48) | (44) | (48) | (46) |
| Intestine Small, Ileum | (43) | (41) | (47) | (45) |
| Intestine Small, Jejunum | (43) | (41) | (48) | (45) |
| Adenoma | | 1 (2%) | | |
| Carcinoma | | 1 (2%) | | |
| Liver | (50) | (50) | (50) | (50) |
| Hepatocellular Adenoma, Multiple | 9 (18%) | 11 (22%) | 14 (28%) | 13 (26%) |
| Hepatocellular Carcinoma, Multiple | 2 (4%) | 2 (4%) | 4 (8%) | 3 (6%) |
| Hepatocellular Adenoma | 15 (30%) | 16 (32%) | 13 (26%) | 12 (24%) |
| Ito Cell Tumor Malignant | 1 (2%) | | | |
| Hepatocellular Carcinoma | 8 (16%) | 10 (20%) | 7 (14%) | 14 (28%) |
| Hemangiosarcoma | 4 (8%) | | | |
| Hepatocholangiocarcinoma | | 1 (2%) | 1 (2%) | 1 (2%) |
| Mesentery | (5) | (3) | (2) | (5) |
| Pancreas | (50) | (48) | (49) | (49) |
| Hepatocholangiocarcinoma, Metastatic, | | 1 (2%) | | 1 (2%) |
| Liver | | | | |
| Stomach, Forestomach | (50) | (49) | (49) | (48) |
| Squamous Cell Papilloma | | 1 (2%) | | 2 (4%) |
| Stomach, Glandular | (48) | (47) | (49) | (47) |
| Tooth | (0) | (1) | (2) | (1) |
| Odontoma | | 1 (100%) | | |
| CARDIOVASCULAR SYSTEM | | | | |

a - Number of animals examined microscopically at site and number of animals with lesion

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Lab: BNW

| B6C3F1 MICE MALE | CONTROL | 100 PPM | 300 PPM | 600 PPM |
|---|---------|---------|---------|---------|
| Heart | (50) | (50) | (50) | (50) |
| Hemangiosarcoma | 1 (2%) | | | |
| Hepatocholangiocarcinoma, Metastatic, Liver | | | 1 (2%) | |
| Alveolar/Bronchiolar Carcinoma, Metastatic, Lung | | | | 1 (2%) |
| ENDOCRINE SYSTEM | | | | |
| Adrenal Cortex | (50) | (49) | (49) | (50) |
| Capsule, Adenoma | | 1 (2%) | 1 (2%) | |
| Capsule, Carcinoma | | 1 (2%) | | |
| Adrenal Medulla | (50) | (49) | (49) | (49) |
| Pheochromocytoma Benign | | 1 (2%) | | 1 (2%) |
| Islets, Pancreatic | (50) | (48) | (49) | (49) |
| Carcinoma | 1 (2%) | | | |
| Pituitary Gland | (48) | (47) | (49) | (45) |
| Pars Intermedia, Adenoma | 1 (2%) | | 1 (2%) | |
| Thyroid Gland | (50) | (50) | (50) | (50) |
| Follicular Cell, Adenoma | 3 (6%) | | 1 (2%) | 2 (4%) |
| Follicular Cell, Carcinoma | | 1 (2%) | | |
| GENERAL BODY SYSTEM | | | | |
| Peritoneum | (0) | (4) | (0) | (0) |
| Hepatocellular Carcinoma, Metastatic, Liver | | 1 (25%) | | |
| Hepatocholangiocarcinoma, Metastatic, Liver | | 1 (25%) | | |
| GENITAL SYSTEM | | | | |
| Epididymis | (50) | (50) | (50) | (50) |
| Prostate | (50) | (49) | (49) | (49) |
| Seminal Vesicle | (49) | (49) | (49) | (45) |
| Testes | (50) | (50) | (50) | (50) |
| Interstitial Cell, Adenoma | | 1 (2%) | | |

a - Number of animals examined microscopically at site and number of animals with lesion

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Pathologist: GRUMBEIN, S.

Lab: BNW

| B6C3F1 MICE MALE | CONTROL | 100 PPM | 300 PPM | 600 PPM |
|---|---------|---------|---------|---------|
| HEMATOPOIETIC SYSTEM | | | | |
| Bone Marrow | (50) | (49) | (50) | (49) |
| Lymph Node | (0) | (4) | (1) | (0) |
| Renal, Hepatocholangiocarcinoma, Metastatic, Liver | | 1 (25%) | | |
| Lymph Node, Bronchial | (42) | (34) | (37) | (33) |
| Hepatocholangiocarcinoma, Metastatic, Liver | | | 1 (3%) | |
| Alveolar/Bronchiolar Carcinoma, Metastatic, Lung | | | | 1 (3%) |
| Lymph Node, Mandibular | (21) | (25) | (28) | (22) |
| Lymph Node, Mediastinal | (41) | (41) | (30) | (32) |
| Hepatocholangiocarcinoma, Metastatic, Liver | | 1 (2%) | 1 (3%) | |
| Alveolar/Bronchiolar Carcinoma, Metastatic, Lung | | | | 1 (3%) |
| Lymph Node, Mesenteric | (48) | (47) | (48) | (47) |
| Hepatocholangiocarcinoma, Metastatic, Liver | | 1 (2%) | | |
| Spleen | (50) | (49) | (49) | (47) |
| Hemangiosarcoma | 1 (2%) | | | |
| Thymus | (41) | (46) | (44) | (40) |
| Alveolar/Bronchiolar Carcinoma, Metastatic, Lung | | | | 1 (3%) |
| INTEGUMENTARY SYSTEM | | | | |
| Skin | (50) | (50) | (50) | (50) |
| Subcutaneous Tissue, Hemangiosarcoma | 1 (2%) | | | |
| Subcutaneous Tissue, Granular Cell Tumor Benign | | | | 1 (2%) |
| MUSCULOSKELETAL SYSTEM | | | | |
| Skeletal Muscle | (0) | (2) | (0) | (0) |
| Hepatocholangiocarcinoma, Metastatic, Liver | | 1 (50%) | | |

a - Number of animals examined microscopically at site and number of animals with lesion

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| B6C3F1 MICE MALE | CONTROL | 100 PPM | 300 PPM | 600 PPM |
|---|----------|---------|----------|----------|
| NERVOUS SYSTEM | | | | |
| None | | | | |
| RESPIRATORY SYSTEM | | | | |
| Lung | (50) | (50) | (50) | (50) |
| Alveolar/Bronchiolar Adenoma | 7 (14%) | 4 (8%) | 7 (14%) | 7 (14%) |
| Hepatocellular Carcinoma, Metastatic, Liver | 4 (8%) | 6 (12%) | 4 (8%) | 7 (14%) |
| Alveolar/Bronchiolar Carcinoma | 5 (10%) | 2 (4%) | 1 (2%) | 1 (2%) |
| Hemangiosarcoma | 1 (2%) | | | |
| Alveolar/Bronchiolar Adenoma, Multiple | 1 (2%) | | 1 (2%) | |
| Hepatocholangiocarcinoma, Metastatic, Liver | | 1 (2%) | 1 (2%) | 1 (2%) |
| Bronchiole, Adenoma, Multiple | | | 1 (2%) | |
| Bronchus, Adenoma | | | | 1 (2%) |
| Alveolar/Bronchiolar Carcinoma, Multiple | | | | 1 (2%) |
| Pleura | (0) | (0) | (1) | (1) |
| Hepatocholangiocarcinoma, Metastatic, Liver | | | 1 (100%) | |
| Alveolar/Bronchiolar Carcinoma, Metastatic, Lung | | | | 1 (100%) |
| SPECIAL SENSES SYSTEM | | | | |
| Harderian Gland | (50) | (49) | (50) | (47) |
| Adenoma | 10 (20%) | 4 (8%) | 3 (6%) | 7 (15%) |
| Carcinoma | 1 (2%) | | 1 (2%) | 2 (4%) |
| URINARY SYSTEM | | | | |
| Kidney | (50) | (49) | (50) | (49) |
| Renal Tubule, Adenoma | | | 1 (2%) | |
| Hepatocellular Carcinoma, Metastatic, Liver | | | | 1 (2%) |
| Urinary Bladder | (50) | (48) | (50) | (48) |

a - Number of animals examined microscopically at site and number of animals with lesion

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| B6C3F1 MICE MALE | CONTROL | 100 PPM | 300 PPM | 600 PPM |
|-------------------------|---------|---------|---------|---------|
| SYSTEMIC LESIONS | | | | |
| Multiple Organs | * (50) | * (50) | * (50) | * (50) |
| Histiocytic Sarcoma | | 2 (4%) | 1 (2%) | 1 (2%) |
| Lymphoma Malignant | | 1 (2%) | 3 (6%) | 1 (2%) |

a - Number of animals examined microscopically at site and number of animals with lesion

* Number of animals with any tissue examined microscopically

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Lab: BNW

| B6C3F1 MICE MALE | CONTROL | 100 PPM | 300 PPM | 600 PPM |
|--|---------|---------|---------|---------|
| Tumor Summary for Males | | | | |
| Total Animals with Primary Neoplasms (b) | 43 | 40 | 37 | 44 |
| Total Primary Neoplasms | 72 | 62 | 61 | 70 |
| Total Animals with Benign Neoplasms | 35 | 31 | 33 | 32 |
| Total Benign Neoplasms | 46 | 41 | 43 | 46 |
| Total Animals with Malignant Neoplasms | 19 | 20 | 17 | 22 |
| Total Malignant Neoplasms | 26 | 21 | 18 | 24 |
| Total Animals with Metastatic Neoplasms | 4 | 7 | 5 | 9 |
| Total Metastatic Neoplasms | 4 | 14 | 9 | 15 |
| Total Animals with Malignant Neoplasms Uncertain Primary Site | | | | |
| Total Animals with Neoplasms Uncertain-Benign or Malignant Total Uncertain Neoplasms | | | | |

*** END OF MALE ***

a - Number of animals examined microscopically at site and number of animals with lesion

b - Primary tumors: all tumors except metastatic tumors

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First Dose M/F: 07/30/01 / 07/30/01

Lab: BNW

| B6C3F1 MICE FEMALE | CONTROL | 100 PPM | 300 PPM | 600 PPM |
|------------------------------------|---------|----------|----------|----------|
| Disposition Summary | | | | |
| Animals Initially in Study | 50 | 50 | 50 | 50 |
| Early Deaths | | | | |
| Accidentally Killed | | | 1 | |
| Moribund Sacrifice | 8 | 9 | 8 | 11 |
| Natural Death | 3 | 3 | 4 | 2 |
| Survivors | | | | |
| Terminal Sacrifice | 39 | 38 | 37 | 37 |
| Animals Examined Microscopically | 50 | 50 | 50 | 50 |
| ALIMENTARY SYSTEM | | | | |
| Gallbladder | (47) | (43) | (41) | (43) |
| Intestine Large, Colon | (49) | (48) | (48) | (50) |
| Intestine Large, Rectum | (48) | (48) | (48) | (50) |
| Leiomyosarcoma | | | 1 (2%) | |
| Intestine Small, Duodenum | (48) | (48) | (46) | (49) |
| Intestine Small, Ileum | (48) | (48) | (46) | (48) |
| Carcinoma | | 1 (2%) | | |
| Intestine Small, Jejunum | (49) | (47) | (46) | (48) |
| Carcinoma | | | 1 (2%) | |
| Liver | (50) | (50) | (50) | (50) |
| Hepatocellular Adenoma | 6 (12%) | 16 (32%) | 9 (18%) | 7 (14%) |
| Hepatocellular Carcinoma | 3 (6%) | 7 (14%) | 6 (12%) | 17 (34%) |
| Hemangioma | 1 (2%) | 1 (2%) | | |
| Hepatocellular Adenoma, Multiple | 4 (8%) | 4 (8%) | 12 (24%) | 16 (32%) |
| Hemangiosarcoma | 1 (2%) | | | |
| Hepatocellular Carcinoma, Multiple | | 2 (4%) | | 1 (2%) |
| Hepatocholangiocarcinoma | | | 1 (2%) | |
| Hepatoblastoma | | | | 1 (2%) |
| Mesentery | (8) | (5) | (5) | (6) |
| Pancreas | (49) | (50) | (49) | (50) |
| Salivary Glands | (50) | (50) | (50) | (50) |
| Stomach, Forestomach | (50) | (50) | (49) | (50) |
| Squamous Cell Papilloma | 1 (2%) | | 1 (2%) | 1 (2%) |
| Stomach, Glandular | (49) | (48) | (49) | (50) |

a - Number of animals examined microscopically at site and number of animals with lesion

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Pathologist: GRUMBEIN, S.

Lab: BNW

| B6C3F1 MICE FEMALE | CONTROL | 100 PPM | 300 PPM | 600 PPM |
|--|---------|---------|---------|---------|
| CARDIOVASCULAR SYSTEM | | | | |
| Heart | (50) | (50) | (50) | (50) |
| Hemangiosarcoma | 1 (2%) | | | |
| Sarcoma, Metastatic, Skin | | 1 (2%) | | |
| Hepatocellular Carcinoma, Metastatic, Liver | | 1 (2%) | | |
| ENDOCRINE SYSTEM | | | | |
| Adrenal Cortex | (50) | (50) | (50) | (50) |
| Capsule, Adenoma | 1 (2%) | | | |
| Hepatocellular Carcinoma, Metastatic, Liver | | | | 1 (2%) |
| Adrenal Medulla | (50) | (50) | (49) | (49) |
| Pheochromocytoma Benign | 2 (4%) | 1 (2%) | 2 (4%) | |
| Pituitary Gland | (50) | (48) | (50) | (47) |
| Pars Distalis, Adenoma | 4 (8%) | 6 (13%) | 4 (8%) | 2 (4%) |
| Pars Intermedia, Adenoma | | | 2 (4%) | |
| Thyroid Gland | (50) | (50) | (50) | (50) |
| Follicular Cell, Adenoma | 3 (6%) | | 1 (2%) | 2 (4%) |
| Follicular Cell, Carcinoma | | 1 (2%) | | |
| Sarcoma, Metastatic, Skin | | 1 (2%) | | |
| GENERAL BODY SYSTEM | | | | |
| None | | | | |
| GENITAL SYSTEM | | | | |
| Clitoral Gland | (43) | (41) | (42) | (41) |
| Squamous Cell Carcinoma | 1 (2%) | | | |
| Ovary | (48) | (50) | (49) | (50) |
| Cystadenoma | 2 (4%) | 1 (2%) | 3 (6%) | 2 (4%) |
| Luteoma | | 1 (2%) | | |
| Hepatocellular Carcinoma, Metastatic, Liver | | | | 1 (2%) |
| Tubulostromal Adenoma | | | | 1 (2%) |

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| B6C3F1 MICE FEMALE | CONTROL | 100 PPM | 300 PPM | 600 PPM |
|--|---------|---------|---------|---------|
| Uterus | (50) | (50) | (49) | (50) |
| Polyp Stromal | 3 (6%) | | 3 (6%) | |
| Leiomyoma | 1 (2%) | | | |
| Hemangiosarcoma | 1 (2%) | | | |
| Endometrium, Adenoma | 1 (2%) | | | |
| HEMATOPOIETIC SYSTEM | | | | |
| Bone Marrow | (50) | (49) | (48) | (50) |
| Lymph Node | (4) | (5) | (2) | (1) |
| Lymph Node, Bronchial | (41) | (41) | (39) | (37) |
| Sarcoma, Metastatic, Skin | | 1 (2%) | | |
| Hepatocholangiocarcinoma, Metastatic, Liver | | | 1 (3%) | |
| Hepatocellular Carcinoma, Metastatic, Liver | | | | 1 (3%) |
| Lymph Node, Mandibular | (40) | (39) | (37) | (36) |
| Lymph Node, Mediastinal | (34) | (40) | (34) | (36) |
| Hepatocholangiocarcinoma, Metastatic, Liver | | | 1 (3%) | |
| Fibrosarcoma, Metastatic, Skin | | | | 1 (3%) |
| Lymph Node, Mesenteric | (48) | (48) | (47) | (50) |
| Spleen | (50) | (50) | (49) | (50) |
| Thymus | (50) | (45) | (49) | (46) |
| Sarcoma, Metastatic, Skin | | 1 (2%) | | |
| INTEGUMENTARY SYSTEM | | | | |
| Mammary Gland | (50) | (50) | (50) | (50) |
| Carcinoma | 1 (2%) | | | |
| Skin | (50) | (50) | (50) | (50) |
| Subcutaneous Tissue, Sarcoma | 6 (12%) | 2 (4%) | | 2 (4%) |
| Subcutaneous Tissue, Liposarcoma | 1 (2%) | | | |
| Subcutaneous Tissue, Hemangiosarcoma | 1 (2%) | | | |
| Subcutaneous Tissue, Fibrosarcoma | | 1 (2%) | | 1 (2%) |
| Subcutaneous Tissue, Sarcoma, Multiple | | | | 1 (2%) |
| Subcutaneous Tissue, Liposarcoma, Multiple | | | | 1 (2%) |

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| B6C3F1 MICE FEMALE | CONTROL | 100 PPM | 300 PPM | 600 PPM |
|--|---------|---------|----------|----------|
| MUSCULOSKELETAL SYSTEM | | | | |
| Skeletal Muscle | (0) | (0) | (1) | (0) |
| Hepatocholangiocarcinoma, Metastatic, Liver | | | 1 (100%) | |
| NERVOUS SYSTEM | | | | |
| Brain | (50) | (50) | (50) | (50) |
| RESPIRATORY SYSTEM | | | | |
| Larynx | (49) | (50) | (49) | (50) |
| Lung | (50) | (50) | (50) | (50) |
| Alveolar/Bronchiolar Adenoma | 1 (2%) | 2 (4%) | 4 (8%) | 4 (8%) |
| Hepatocellular Carcinoma, Metastatic, Liver | 1 (2%) | 5 (10%) | 3 (6%) | 13 (26%) |
| Alveolar/Bronchiolar Carcinoma | 1 (2%) | 5 (10%) | 1 (2%) | 2 (4%) |
| Sarcoma, Metastatic, Skin | | 1 (2%) | | 2 (4%) |
| Hepatocholangiocarcinoma, Metastatic, Liver | | | 1 (2%) | |
| Alveolar/Bronchiolar Carcinoma, Multiple Fibrosarcoma, Metastatic, Skin | | | 1 (2%) | 1 (2%) |
| Nose | (49) | (49) | (50) | (50) |
| Trachea | (49) | (50) | (50) | (50) |
| SPECIAL SENSES SYSTEM | | | | |
| Eye | (50) | (47) | (46) | (49) |
| Harderian Gland | (50) | (48) | (48) | (50) |
| Adenoma | 3 (6%) | 3 (6%) | 3 (6%) | 1 (2%) |
| Carcinoma | 1 (2%) | | | 1 (2%) |
| URINARY SYSTEM | | | | |
| Kidney | (50) | (49) | (50) | (50) |
| Urinary Bladder | (49) | (48) | (48) | (50) |

a - Number of animals examined microscopically at site and number of animals with lesion

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Species/Strain: MICE/B6C3F1

Lab: BNW

| B6C3F1 MICE FEMALE | CONTROL | 100 PPM | 300 PPM | 600 PPM |
|---------------------|----------|---------|----------|---------|
| SYSTEMIC LESIONS | | | | |
| Multiple Organs | * (50) | * (50) | * (50) | * (50) |
| Histiocytic Sarcoma | 1 (2%) | 1 (2%) | 3 (6%) | 1 (2%) |
| Lymphoma Malignant | 15 (30%) | 6 (12%) | 11 (22%) | 4 (8%) |

a - Number of animals examined microscopically at site and number of animals with lesion

* Number of animals with any tissue examined microscopically

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| B6C3F1 MICE FEMALE | CONTROL | 100 PPM | 300 PPM | 600 PPM |
|--------------------|---------|---------|---------|---------|
|--------------------|---------|---------|---------|---------|

Tumor Summary for Females

| | | | | |
|--|----|----|----|----|
| Total Animals with Primary Neoplasms (b) | 40 | 36 | 42 | 41 |
| Total Primary Neoplasms | 67 | 61 | 69 | 68 |
| Total Animals with Benign Neoplasms | 26 | 29 | 35 | 27 |
| Total Benign Neoplasms | 33 | 35 | 44 | 36 |
| Total Animals with Malignant Neoplasms | 29 | 21 | 22 | 25 |
| Total Malignant Neoplasms | 34 | 26 | 25 | 32 |
| Total Animals with Metastatic Neoplasms | 1 | 6 | 4 | 16 |
| Total Metastatic Neoplasms | 1 | 11 | 7 | 20 |
| Total Animals with Malignant Neoplasms Uncertain Primary Site | | | | |
| Total Animals with Neoplasms Uncertain-Benign or Malignant Total Uncertain Neoplasms | | | | |

*** END OF REPORT ***

a - Number of animals examined microscopically at site and number of animals with lesion

b - Primary tumors: all tumors except metastatic tumors