

**TDMs No.** 97003 - 08

**P18: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE (a) WITH  
AVERAGE SEVERITY GRADES[b]**

**Date Report Requested:** 08/21/2007

**Test Type:** CHRONIC

1,2-Dibromo-2,4-dicyanobutane

**Time Report Requested:** 13:25:49

**Route:** SKIN APPLICATION

**CAS Number:** 35691-65-7

**First Dose M/F:** 06/25/02 / 06/24/02

**Species/Strain:** MICE/B6C3F1

**Lab:** BAT

F\_1.Rev.1\_M3

**C Number:** C97003D

**Lock Date:** 01/31/2005

**Cage Range:** ALL

**Date Range:** ALL

**Reasons For Removal:** ALL

**Removal Date Range:** ALL

**Treatment Groups:** Include ALL

**TDMSE Version:** 1.8.0

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First Dose M/F: 06/25/02 / 06/24/02

Species/Strain: MICE/B6C3F1

Lab: BAT

| B6C3F1 MICE MALE                 | 0 MG/KG | 0.6 MG/KG | 2 MG/KG | 6 MG/KG |
|----------------------------------|---------|-----------|---------|---------|
| <b>Disposition Summary</b>       |         |           |         |         |
| Animals Initially in Study       | 50      | 50        | 50      | 50      |
| Early Deaths                     |         |           |         |         |
| Accidently Killed                |         | 1         |         |         |
| Moribund Sacrifice               | 8       | 12        | 8       | 7       |
| Natural Death                    | 7       | 7         | 3       | 3       |
| Survivors                        |         |           |         |         |
| Moribund Sacrifice               | 1       |           |         |         |
| Terminal Sacrifice               | 34      | 30        | 39      | 40      |
| Animals Examined Microscopically | 50      | 50        | 50      | 50      |

## ALIMENTARY SYSTEM

|   |          |          |          |          |
|---|----------|----------|----------|----------|
| Esophagus                               | (50)     | (50)     | (50)     | (50)     |
| Gallbladder                             | (49)     | (49)     | (48)     | (49)     |
| Inflammation                            | 3 [1.0]  |          | 3 [1.0]  | 2 [1.0]  |
| Intestine Large, Cecum                  | (50)     | (50)     | (50)     | (50)     |
| Hyperplasia, Lymphoid                   |          |          |          | 1 [3.0]  |
| Intestine Large, Colon                  | (50)     | (50)     | (50)     | (50)     |
| Intestine Large, Rectum                 | (50)     | (50)     | (50)     | (50)     |
| Intestine Small, Duodenum               | (50)     | (50)     | (50)     | (50)     |
| Ectopic Tissue                          |          |          | 1 [3.0]  |          |
| Intestine Small, Ileum                  | (50)     | (49)     | (50)     | (50)     |
| Inflammation                            | 1 [3.0]  |          |          |          |
| Ulcer                                   | 1 [3.0]  |          |          |          |
| Peyer's Patch, Hyperplasia, Lymphoid    | 1 [4.0]  |          |          |          |
| Intestine Small, Jejunum                | (50)     | (50)     | (50)     | (50)     |
| Peyer's Patch, Hyperplasia, Lymphoid    |          | 1 [4.0]  | 4 [3.3]  | 2 [3.0]  |
| Liver                                   | (50)     | (50)     | (50)     | (50)     |
| Basophilic Focus                        | 1        | 4        | 5        | 4        |
| Clear Cell Focus                        | 34       | 22       | 29       | 24       |
| Eosinophilic Focus                      | 21       | 9        | 16       | 16       |
| Fatty Change, Focal                     | 11 [1.4] |          | 4 [1.5]  | 6 [1.7]  |
| Fatty Change, Diffuse                   | 19 [1.2] | 15 [1.1] | 11 [1.0] | 14 [1.0] |
| Hematopoietic Cell Proliferation        | 3 [1.3]  | 9 [1.3]  | 2 [1.0]  | 1 [1.0]  |
| Infarct                                 | 1 [4.0]  |          |          |          |
| Infiltration Cellular, Mononuclear Cell | 1 [2.0]  |          |          |          |

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

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

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1,2-Dibromo-2,4-dicyanobutane

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Species/Strain: MICE/B6C3F1

Lab: BAT

| B6C3F1 MICE MALE                        | 0 MG/KG  | 0.6 MG/KG | 2 MG/KG  | 6 MG/KG  |
|---|----------|-----------|----------|----------|
| Inflammation                            | 31 [1.0] | 19 [1.1]  | 27 [1.0] | 28 [1.0] |
| Mineralization                          | 1 [2.0]  |           |          |          |
| Mixed Cell Focus                        | 14       | 9         | 13       | 12       |
| Necrosis                                | 3 [1.7]  | 9 [1.9]   | 5 [1.8]  | 7 [2.0]  |
| Pigmentation                            | 4 [1.8]  | 3 [1.3]   |          |          |
| Tension Lipidosis                       | 3        | 5         | 3 [1.0]  | 3 [1.0]  |
| Bile Duct, Cyst                         | 1 [3.0]  |           |          |          |
| Hepatocyte, Hypertrophy                 |          | 1 [2.0]   |          |          |
| Mesentery                               | (10)     | (3)       | (4)      | (2)      |
| Fat, Necrosis                           | 9 [2.9]  | 3 [3.0]   | 3 [3.0]  | 1 [3.0]  |
| Pancreas                                | (50)     | (50)      | (50)     | (50)     |
| Hyperplasia                             | 1 [1.0]  |           |          |          |
| Infiltration Cellular, Mononuclear Cell | 7 [1.0]  |           | 3 [1.0]  | 6 [1.2]  |
| Inflammation                            | 2 [2.0]  |           |          |          |
| Vacuolization Cytoplasmic               |          |           |          | 1 [2.0]  |
| Acinus, Atrophy                         |          | 2 [1.0]   |          | 1 [2.0]  |
| Duct, Cyst                              |          |           |          | 1 [4.0]  |
| Salivary Glands                         | (50)     | (50)      | (50)     | (50)     |
| Atrophy                                 |          | 1 [2.0]   |          | 1 [2.0]  |
| Infiltration Cellular, Mononuclear Cell | 35 [1.6] | 28 [1.5]  | 39 [1.5] | 40 [1.8] |
| Necrosis                                |          | 1 [2.0]   |          |          |
| Stomach, Forestomach                    | (50)     | (50)      | (50)     | (50)     |
| Hyperplasia, Squamous                   | 1 [1.0]  | 1 [2.0]   | 1 [1.0]  | 1 [2.0]  |
| Inflammation                            | 2 [1.0]  |           |          |          |
| Ulcer                                   |          |           |          | 2 [2.0]  |
| Stomach, Glandular                      | (50)     | (50)      | (50)     | (50)     |
| Cyst                                    |          |           | 1 [1.0]  |          |
| Erosion                                 |          | 1 [3.0]   | 1 [1.0]  | 1 [2.0]  |
| Inflammation                            | 1 [2.0]  | 1 [1.0]   |          |          |
| Mineralization                          |          |           |          | 1 [2.0]  |
| Glands, Cyst                            | 1 [1.0]  | 1 [2.0]   |          | 2 [1.5]  |
| Glands, Hyperplasia                     | 1 [2.0]  | 1 [3.0]   | 2 [2.5]  |          |
| Tooth                                   | (31)     | (32)      | (37)     | (35)     |
| Dysplasia                               |          |           | 2        | 1        |
| Malformation                            | 29 [1.4] | 32 [1.7]  | 36 [1.4] | 33 [1.8] |
| Peridontal Tissue, Inflammation         | 7 [1.7]  | 2 [2.0]   | 1 [2.0]  | 9 [2.0]  |
| Pulp, Inflammation                      | 2 [1.5]  |           |          |          |

## CARDIOVASCULAR SYSTEM

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

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

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1,2-Dibromo-2,4-dicyanobutane

Time Report Requested: 13:25:49

Route: SKIN APPLICATION

CAS Number: 35691-65-7

First Dose M/F: 06/25/02 / 06/24/02

Species/Strain: MICE/B6C3F1

Lab: BAT

| B6C3F1 MICE MALE                        | 0 MG/KG  | 0.6 MG/KG | 2 MG/KG  | 6 MG/KG  |
|---|----------|-----------|----------|----------|
| Blood Vessel                            | (50)     | (50)      | (50)     | (50)     |
| Heart                                   | (50)     | (50)      | (50)     | (50)     |
| Cardiomyopathy                          | 9 [1.3]  | 6 [1.2]   | 5 [1.0]  | 3 [1.3]  |
| Infiltration Cellular, Mononuclear Cell | 1 [2.0]  |           |          |          |
| Inflammation                            |          | 1 [1.0]   |          |          |
| Mineralization                          |          | 1 [1.0]   |          |          |
| Capillary, Hyperplasia                  |          |           | 1 [2.0]  |          |
| <b>ENDOCRINE SYSTEM</b>                 |          |           |          |          |
| Adrenal Cortex                          | (50)     | (50)      | (50)     | (50)     |
| Cytoplasmic Alteration                  |          | 1 [2.0]   |          |          |
| Degeneration                            | 1 [4.0]  |           |          |          |
| Hypertrophy                             | 22 [1.7] | 16 [1.6]  | 23 [1.5] | 21 [1.8] |
| Pigmentation                            | 2 [1.5]  |           |          |          |
| Vacuolization Cytoplasmic               | 1 [2.0]  | 1 [1.0]   | 1 [1.0]  |          |
| Subcapsular, Hyperplasia                | 45 [1.8] | 46 [1.8]  | 46 [1.9] | 44 [1.7] |
| Zona Fasciculata, Hyperplasia           | 6 [2.0]  |           | 1 [1.0]  | 5 [1.4]  |
| Adrenal Medulla                         | (50)     | (49)      | (50)     | (50)     |
| Hyperplasia                             |          | 2 [2.5]   |          |          |
| Islets, Pancreatic                      | (50)     | (50)      | (50)     | (50)     |
| Hyperplasia                             | 26 [1.5] | 23 [1.4]  | 28 [1.4] | 25 [1.3] |
| Parathyroid Gland                       | (42)     | (40)      | (43)     | (41)     |
| Cyst                                    |          |           | 1 [2.0]  |          |
| Pituitary Gland                         | (50)     | (50)      | (49)     | (50)     |
| Cyst                                    | 3 [1.7]  | 3 [1.7]   | 4 [1.0]  | 6 [1.5]  |
| Hyperplasia                             | 1 [2.0]  | 1 [2.0]   | 1 [1.0]  |          |
| Thyroid Gland                           | (50)     | (50)      | (50)     | (50)     |
| Cyst                                    | 1 [2.0]  |           |          |          |
| Infiltration Cellular, Mononuclear Cell |          |           | 1 [1.0]  |          |
| C-cell, Hyperplasia                     |          |           |          | 1 [2.0]  |
| Follicle, Cyst                          | 1 [1.0]  |           | 2 [3.0]  |          |
| Follicular Cell, Hyperplasia            |          | 3 [1.7]   | 2 [2.5]  | 1 [2.0]  |
| <b>GENERAL BODY SYSTEM</b>              |          |           |          |          |
| None                                    |          |           |          |          |

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Lab: BAT

| B6C3F1 MICE MALE                        | 0 MG/KG  | 0.6 MG/KG | 2 MG/KG  | 6 MG/KG  |
|---|----------|-----------|----------|----------|
| <b>GENITAL SYSTEM</b>                   |          |           |          |          |
| Coagulating Gland                       | (0)      | (1)       | (2)      | (1)      |
| Hyperplasia                             |          |           | 1 [2.0]  |          |
| Inflammation                            |          |           | 1 [2.0]  |          |
| Epididymis                              | (50)     | (50)      | (50)     | (50)     |
| Granuloma Sperm                         |          |           | 2 [2.5]  | 2 [2.5]  |
| Inflammation                            | 37 [1.1] | 35 [1.0]  | 35 [1.1] | 34 [1.0] |
| Penis                                   | (0)      | (2)       | (0)      | (0)      |
| Congestion                              |          | 1 [2.0]   |          |          |
| Preputial Gland                         | (50)     | (50)      | (50)     | (50)     |
| Infiltration Cellular, Mononuclear Cell |          |           |          | 1 [3.0]  |
| Inflammation                            | 38 [1.4] | 30 [1.6]  | 26 [1.4] | 28 [1.4] |
| Duct, Ectasia                           | 2 [2.0]  | 2 [2.5]   | 1 [2.0]  | 4 [2.3]  |
| Prostate                                | (50)     | (50)      | (50)     | (50)     |
| Atrophy                                 |          |           |          | 1 [3.0]  |
| Infiltration Cellular, Mononuclear Cell | 20 [1.2] | 17 [1.1]  | 18 [1.1] | 14 [1.3] |
| Inflammation, Suppurative               |          |           | 1 [3.0]  |          |
| Seminal Vesicle                         | (50)     | (50)      | (50)     | (50)     |
| Atrophy                                 |          |           |          | 1 [3.0]  |
| Testes                                  | (50)     | (50)      | (50)     | (50)     |
| Mineralization                          | 1 [2.0]  |           | 3 [1.0]  | 1 [1.0]  |
| Germinal Epithelium, Atrophy            | 4 [1.8]  |           | 3 [2.0]  | 5 [2.2]  |
| <b>HEMATOPOIETIC SYSTEM</b>             |          |           |          |          |
| Bone Marrow                             | (50)     | (50)      | (50)     | (50)     |
| Angiectasis                             | 1 [2.0]  |           |          |          |
| Myelofibrosis                           |          | 2 [1.5]   | 2 [1.0]  | 1 [3.0]  |
| Myeloid Cell, Hyperplasia               | 3 [2.3]  | 4 [2.5]   | 3 [2.0]  | 3 [2.0]  |
| Lymph Node                              | (0)      | (1)       | (3)      | (1)      |
| Renal, Hyperplasia, Lymphoid            |          |           | 1 [4.0]  |          |
| Lymph Node, Mandibular                  | (50)     | (50)      | (50)     | (50)     |
| Atrophy                                 | 1 [3.0]  |           |          | 1 [3.0]  |
| Hemorrhage                              |          | 1 [2.0]   |          |          |
| Hyperplasia, Lymphoid                   | 2 [2.0]  | 1 [2.0]   |          | 1 [2.0]  |
| Hyperplasia, Plasma Cell                |          | 4 [2.0]   | 1 [2.0]  |          |
| Pigmentation                            | 1 [2.0]  | 1 [2.0]   |          |          |
| Lymph Node, Mesenteric                  | (50)     | (50)      | (50)     | (50)     |

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Lab: BAT

| B6C3F1 MICE MALE  | 0 MG/KG  | 0.6 MG/KG | 2 MG/KG  | 6 MG/KG  |
|---|----------|-----------|----------|----------|
| Atrophy   | 1 [3.0]  | 1 [2.0]   | 1 [3.0]  | 1 [2.0]  |
| Hemorrhage  | 1 [2.0]  |           | 1 [2.0]  | 1 [2.0]  |
| Hyperplasia, Histiocytic                                      |          |           | 1 [2.0]  |          |
| Hyperplasia, Lymphoid   | 1 [4.0]  | 2 [3.5]   | 1 [3.0]  | 1 [2.0]  |
| Hyperplasia, Plasma Cell                                      |          | 2 [2.5]   |          |          |
| Inflammation, Suppurative                                     | 1 [3.0]  |           |          |          |
| Inflammation, Granulomatous                                   | 1 [3.0]  |           |          |          |
| Spleen  | (50)     | (49)      | (50)     | (50)     |
| Hematopoietic Cell Proliferation                              | 19 [2.3] | 13 [2.5]  | 20 [2.2] | 13 [2.5] |
| Hyperplasia, Histiocytic                                      |          |           |          | 1 [3.0]  |
| Hyperplasia, Lymphoid   | 8 [2.1]  | 12 [2.1]  | 12 [1.8] | 11 [2.4] |
| Infiltration Cellular, Polymorphonuclear                      |          |           | 1 [3.0]  |          |
| Capsule, Degeneration   | 1 [2.0]  |           |          |          |
| Lymphoid Follicle, Atrophy                                    | 2 [2.5]  | 4 [2.5]   |          | 1 [2.0]  |
| Red Pulp, Atrophy   | 1 [3.0]  | 4 [2.5]   | 1 [2.0]  | 2 [2.5]  |
| Thymus  | (47)     | (48)      | (46)     | (46)     |
| Atrophy   | 22 [2.5] | 19 [2.5]  | 27 [2.4] | 23 [2.5] |
| Cyst  |          | 2 [1.0]   |          | 1 [2.0]  |
| <b>INTEGUMENTARY SYSTEM</b>                                   |          |           |          |          |
| Skin  | (50)     | (50)      | (50)     | (50)     |
| Hyperplasia   |          |           | 1 [2.0]  |          |
| Inflammation  |          |           | 2 [2.0]  |          |
| Inflammation, Chronic Active                                  | 1 [3.0]  |           |          |          |
| Ulcer   | 1 [3.0]  |           | 2 [3.0]  |          |
| Site Of Application - Dermis,<br>Inflammation, Chronic Active | 4 [1.3]  | 1 [1.0]   | 7 [1.1]  | 10 [1.6] |
| Site Of Application - Epidermis,<br>Hyperplasia               | 6 [2.0]  | 12 [1.0]  | 37 [1.1] | 50 [1.6] |
| Site Of Application - Epidermis, Ulcer                        |          |           | 1 [1.0]  | 3 [2.7]  |
| <b>MUSCULOSKELETAL SYSTEM</b>                                 |          |           |          |          |
| Bone  | (50)     | (50)      | (50)     | (50)     |
| Osteosclerosis  | 1 [2.0]  |           |          |          |
| Skeletal Muscle   | (0)      | (0)       | (1)      | (0)      |

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Lab: BAT

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|--|---------|-----------|---------|---------|
| <b>NERVOUS SYSTEM</b>                                |         |           |         |         |
| Brain  | (50)    | (50)      | (50)    | (50)    |
| Hemorrhage   |         | 1 [2.0]   |         |         |
| Meninges, Infiltration Cellular,<br>Mononuclear Cell |         |           | 1 [1.0] | 1 [2.0] |
| Spinal Cord  | (0)     | (0)       | (0)     | (1)     |
| Atrophy  |         |           |         | 1 [2.0] |
| <b>RESPIRATORY SYSTEM</b>                            |         |           |         |         |
| Lung   | (50)    | (50)      | (50)    | (50)    |
| Hemorrhage   |         | 1 [3.0]   |         | 1 [2.0] |
| Infiltration Cellular, Mononuclear Cell              | 1 [3.0] |           |         |         |
| Inflammation   | 6 [1.7] | 5 [2.2]   |         | 1 [2.0] |
| Pigmentation   | 1 [2.0] | 1 [1.0]   |         |         |
| Thrombosis   | 1 [2.0] |           |         |         |
| Alveolar Epithelium, Hyperplasia                     | 6 [1.7] |           |         | 4 [2.8] |
| Alveolus, Infiltration Cellular, Histiocyte          | 5 [2.2] | 8 [1.8]   | 2 [2.0] | 3 [1.3] |
| Bronchiole, Hyperplasia                              |         |           | 1 [2.0] | 1 [2.0] |
| Nose   | (50)    | (50)      | (50)    | (50)    |
| Inflammation, Suppurative                            |         | 3 [2.3]   |         |         |
| Polyp, Inflammatory                                  | 1 [3.0] |           | 1 [3.0] |         |
| Glands, Dilatation                                   |         |           | 1 [2.0] |         |
| Nerve, Atrophy                                       |         |           | 1 [2.0] |         |
| Respiratory Epithelium, Hyperplasia                  |         |           | 1 [1.0] |         |
| Respiratory Epithelium, Inflammation                 | 7 [1.4] |           | 1 [1.0] |         |
| Respiratory Epithelium, Metaplasia                   |         | 1 [3.0]   |         |         |
| Trachea  | (50)    | (50)      | (50)    | (50)    |
| Inflammation   |         |           |         | 1 [1.0] |
| Glands, Cyst   | 1 [1.0] |           |         |         |
| <b>SPECIAL SENSES SYSTEM</b>                         |         |           |         |         |
| Eye  | (50)    | (50)      | (50)    | (50)    |
| Atrophy  |         | 1 [4.0]   |         |         |
| Cornea, Inflammation                                 |         |           |         | 2 [1.0] |
| Lens, Degeneration                                   | 1 [3.0] | 1 [3.0]   |         |         |
| Retina, Atrophy                                      | 2 [4.0] | 1 [2.0]   |         |         |

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Lab: BAT

| B6C3F1 MICE MALE                        | 0 MG/KG  | 0.6 MG/KG | 2 MG/KG  | 6 MG/KG  |
|---|----------|-----------|----------|----------|
| Harderian Gland                         | (50)     | (50)      | (50)     | (50)     |
| Fibrosis, Focal                         |          | 1 [3.0]   |          |          |
| Infiltration Cellular, Mononuclear Cell | 31 [1.2] | 30 [1.2]  | 26 [1.2] | 30 [1.1] |
| Inflammation                            | 1 [2.0]  |           | 1 [3.0]  |          |
| Epithelium, Hyperplasia                 | 2 [2.0]  | 3 [1.0]   |          | 4 [2.0]  |
| <b>URINARY SYSTEM</b>                   |          |           |          |          |
| Kidney                                  | (50)     | (50)      | (50)     | (50)     |
| Cyst                                    | 3 [1.0]  | 8 [1.8]   | 2 [1.5]  | 6 [1.3]  |
| Hemorrhage                              |          |           |          | 1 [3.0]  |
| Infarct                                 | 4 [1.8]  | 1 [1.0]   | 4 [1.8]  | 3 [1.7]  |
| Infiltration Cellular, Mononuclear Cell | 1 [2.0]  | 1 [3.0]   |          |          |
| Inflammation                            | 2 [3.0]  |           |          |          |
| Mineralization                          | 44 [1.0] | 45 [1.0]  | 46 [1.0] | 43 [1.0] |
| Nephropathy                             | 48 [1.5] | 41 [1.2]  | 48 [1.1] | 48 [1.6] |
| Papilla, Renal Tubule, Necrosis         |          | 1 [3.0]   |          |          |
| Renal Tubule, Hyperplasia               | 12 [1.0] | 12 [1.0]  | 12 [1.0] | 7 [1.0]  |
| Urinary Bladder                         | (50)     | (50)      | (50)     | (50)     |
| Infiltration Cellular, Mononuclear Cell | 22 [1.2] | 19 [1.2]  | 23 [1.0] | 27 [1.2] |
| Transitional Epithelium, Hyperplasia    |          |           | 2 [2.0]  |          |

\*\*\* END OF MALE \*\*\*



Test Type: CHRONIC

1,2-Dibromo-2,4-dicyanobutane

Time Report Requested: 13:25:49

Route: SKIN APPLICATION

CAS Number: 35691-65-7

First Dose M/F: 06/25/02 / 06/24/02

Species/Strain: MICE/B6C3F1

Lab: BAT

| B6C3F1 MICE FEMALE               | 0 MG/KG | 0.6 MG/KG | 2 MG/KG | 6 MG/KG |
|----------------------------------|---------|-----------|---------|---------|
| <b>Disposition Summary</b>       |         |           |         |         |
| Animals Initially in Study       | 50      | 50        | 50      | 50      |
| Early Deaths                     |         |           |         |         |
| Moribund Sacrifice               | 10      | 11        | 14      | 11      |
| Natural Death                    | 7       | 3         | 6       | 4       |
| Survivors                        |         |           |         |         |
| Natural Death                    |         | 1         |         |         |
| Terminal Sacrifice               | 33      | 35        | 30      | 35      |
| Animals Examined Microscopically | 50      | 50        | 50      | 50      |

**ALIMENTARY SYSTEM**

|                                   |          |          |          |          |
|-----------------------------------|----------|----------|----------|----------|
| Esophagus                         | (50)     | (50)     | (50)     | (50)     |
| Gallbladder                       | (50)     | (49)     | (50)     | (50)     |
| Cyst                              |          | 1 [1.0]  |          |          |
| Inflammation                      |          | 3 [1.7]  | 5 [1.0]  | 2 [1.0]  |
| Intestine Small, Duodenum         | (50)     | (50)     | (50)     | (50)     |
| Intestine Small, Jejunum          | (50)     | (50)     | (50)     | (50)     |
| Hyperplasia, Lymphoid             |          |          | 1 [3.0]  |          |
| Inflammation                      | 3 [2.7]  | 1 [1.0]  |          |          |
| Necrosis, Fatty                   | 1 [3.0]  |          |          |          |
| Liver                             | (50)     | (50)     | (50)     | (50)     |
| Angiectasis                       |          | 1 [2.0]  | 1 [1.0]  |          |
| Basophilic Focus                  | 1        | 3        |          |          |
| Clear Cell Focus                  | 14       | 13       | 3        | 8        |
| Cyst                              |          | 1 [2.0]  |          |          |
| Eosinophilic Focus                | 6        | 3        | 4        | 4        |
| Fatty Change, Focal               | 1 [2.0]  |          | 1 [2.0]  |          |
| Fatty Change, Diffuse             | 1 [1.0]  |          | 4 [1.5]  | 4 [2.8]  |
| Fibrosis                          |          | 1 [3.0]  |          |          |
| Hematopoietic Cell Proliferation  | 6 [1.5]  | 3 [1.0]  | 3 [1.0]  | 5 [1.0]  |
| Infiltration Cellular, Lymphocyte |          |          | 1 [2.0]  |          |
| Inflammation                      | 35 [1.2] | 42 [1.2] | 37 [1.1] | 41 [1.1] |
| Mixed Cell Focus                  | 13       | 10       | 5        | 7        |
| Necrosis                          | 3 [2.0]  | 2 [2.0]  | 8 [1.9]  | 4 [2.0]  |
| Pigmentation                      | 4 [1.3]  | 4 [1.5]  | 1 [1.0]  | 1 [1.0]  |
| Tension Lipidosis                 | 5        | 2        | 4        | 6        |

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

b - Average severity grade (1-minimal; 2-mild; 3-moderate; 4-marked)

Test Type: CHRONIC

1,2-Dibromo-2,4-dicyanobutane

Time Report Requested: 13:25:49

Route: SKIN APPLICATION

CAS Number: 35691-65-7

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Species/Strain: MICE/B6C3F1

Lab: BAT

| B6C3F1 MICE FEMALE                                   | 0 MG/KG  | 0.6 MG/KG | 2 MG/KG  | 6 MG/KG  |
|--|----------|-----------|----------|----------|
| Vacuolization Cytoplasmic<br>Hepatocyte, Hypertrophy | 1 [3.0]  |           | 1 [1.0]  |          |
| Mesentery  | (10)     | (9)       | (6)      | (10)     |
| Fat, Necrosis  | 9 [3.0]  | 9 [3.0]   | 6 [3.0]  | 9 [3.0]  |
| Pancreas   | (50)     | (50)      | (50)     | (50)     |
| Cyst   | 1 [2.0]  | 2 [3.0]   |          |          |
| Infiltration Cellular, Mononuclear Cell              | 17 [1.0] | 15 [1.1]  | 17 [1.1] | 24 [1.3] |
| Inflammation   |          | 3 [1.7]   |          |          |
| Acinus, Atrophy                                      | 1 [2.0]  | 3 [3.3]   |          |          |
| Salivary Glands                                      | (50)     | (50)      | (50)     | (50)     |
| Infiltration Cellular, Mononuclear Cell              | 31 [1.5] | 32 [1.3]  | 33 [1.5] | 36 [1.5] |
| Stomach, Forestomach                                 | (50)     | (50)      | (50)     | (50)     |
| Cyst   | 1 [1.0]  |           |          |          |
| Hyperkeratosis                                       | 1 [2.0]  |           |          | 2 [2.5]  |
| Hyperplasia, Squamous                                | 2 [1.5]  |           |          | 2 [2.0]  |
| Inflammation   |          |           |          | 2 [2.0]  |
| Ulcer  |          |           |          | 2 [2.0]  |
| Stomach, Glandular                                   | (50)     | (50)      | (50)     | (50)     |
| Cyst   | 1 [1.0]  |           |          |          |
| Erosion  |          | 2 [2.0]   |          | 1 [2.0]  |
| Mineralization                                       |          |           | 1 [1.0]  | 1 [2.0]  |
| Glands, Cyst   | 2 [1.5]  | 5 [1.0]   | 4 [1.0]  | 5 [1.0]  |
| Glands, Hyperplasia                                  |          | 1 [2.0]   |          |          |
| Tooth  | (3)      | (4)       | (4)      | (1)      |
| Malformation   | 3 [1.3]  | 3 [1.0]   | 3 [1.0]  | 1 [1.0]  |
| Peridontal Tissue, Inflammation                      |          | 1 [2.0]   | 1 [2.0]  |          |
| <b>CARDIOVASCULAR SYSTEM</b>                         |          |           |          |          |
| Blood Vessel   | (50)     | (50)      | (50)     | (50)     |
| Hyperplasia  |          | 1 [2.0]   |          |          |
| Heart  | (50)     | (50)      | (50)     | (50)     |
| Cardiomyopathy                                       | 10 [1.0] | 2 [1.0]   | 9 [1.0]  | 14 [1.0] |
| Infiltration Cellular, Mononuclear Cell              | 1 [1.0]  |           | 1 [1.0]  | 1 [2.0]  |
| Inflammation   |          |           |          | 2 [2.0]  |
| Mineralization                                       | 1 [2.0]  |           |          |          |
| Thrombosis   |          |           |          | 1 [3.0]  |
| <b>ENDOCRINE SYSTEM</b>                              |          |           |          |          |

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Test Type: CHRONIC

1,2-Dibromo-2,4-dicyanobutane

Time Report Requested: 13:25:49

Route: SKIN APPLICATION

CAS Number: 35691-65-7

First Dose M/F: 06/25/02 / 06/24/02

Species/Strain: MICE/B6C3F1

Lab: BAT

| B6C3F1 MICE FEMALE                      | 0 MG/KG  | 0.6 MG/KG | 2 MG/KG  | 6 MG/KG  |
|---|----------|-----------|----------|----------|
| Adrenal Cortex                          | (50)     | (50)      | (50)     | (50)     |
| Hematopoietic Cell Proliferation        | 2 [2.0]  |           |          | 1 [2.0]  |
| Hypertrophy                             | 2 [2.0]  | 2 [1.5]   |          | 1 [2.0]  |
| Inflammation                            | 1 [2.0]  |           |          | 1 [3.0]  |
| Vacuolization Cytoplasmic               |          |           | 1 [3.0]  | 1 [3.0]  |
| Capsule, Necrosis, Fatty                | 1 [2.0]  |           |          |          |
| Subcapsular, Hyperplasia                | 50 [2.5] | 49 [2.3]  | 50 [2.2] | 49 [2.3] |
| Zona Fasciculata, Hyperplasia           | 2 [1.5]  | 2 [1.5]   | 1 [2.0]  | 1 [2.0]  |
| Adrenal Medulla                         | (50)     | (50)      | (50)     | (50)     |
| Hyperplasia                             | 1 [2.0]  | 2 [1.0]   |          | 3 [2.0]  |
| Vacuolization Cytoplasmic               |          |           |          | 1 [3.0]  |
| Islets, Pancreatic                      | (50)     | (50)      | (50)     | (50)     |
| Hyperplasia                             | 4 [1.3]  |           |          | 1 [1.0]  |
| Parathyroid Gland                       | (38)     | (40)      | (40)     | (41)     |
| Cyst                                    |          |           |          | 1 [1.0]  |
| Inflammation, Chronic Active            |          |           |          | 1 [2.0]  |
| Pituitary Gland                         | (50)     | (50)      | (50)     | (50)     |
| Angiectasis                             | 1 [2.0]  | 2 [2.0]   | 1 [2.0]  | 1 [3.0]  |
| Cyst                                    | 1 [1.0]  | 1 [1.0]   |          | 2 [1.0]  |
| Pars Distalis, Angiectasis              |          | 1 [2.0]   |          |          |
| Pars Distalis, Hyperplasia              | 9 [1.6]  | 13 [2.2]  | 16 [1.9] | 12 [2.3] |
| Pars Intermedia, Hyperplasia            |          | 1 [1.0]   |          |          |
| Thyroid Gland                           | (50)     | (50)      | (50)     | (50)     |
| Infiltration Cellular, Mononuclear Cell | 3 [1.0]  | 2 [1.0]   | 3 [1.0]  | 3 [1.3]  |
| Inflammation, Suppurative               | 1 [1.0]  |           |          |          |
| C-cell, Hyperplasia                     |          | 1 [1.0]   |          |          |
| Follicle, Cyst                          | 2 [1.5]  |           |          |          |
| Follicular Cell, Hyperplasia            | 1 [1.0]  | 3 [1.7]   | 1 [2.0]  | 1 [4.0]  |
| Follicular Cell, Hypertrophy            | 1 [1.0]  |           |          |          |

## GENERAL BODY SYSTEM

None

## GENITAL SYSTEM

|                |          |         |         |         |
|----------------|----------|---------|---------|---------|
| Clitoral Gland | (50)     | (49)    | (50)    | (50)    |
| Inflammation   | 18 [1.0] | 5 [1.0] | 2 [1.0] | 7 [1.1] |
| Duct, Cyst     |          |         | 1 [1.0] |         |

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1,2-Dibromo-2,4-dicyanobutane

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Species/Strain: MICE/B6C3F1

Lab: BAT

| B6C3F1 MICE FEMALE                    | 0 MG/KG  | 0.6 MG/KG | 2 MG/KG  | 6 MG/KG  |
|---------------------------------------|----------|-----------|----------|----------|
| Ovary                                 | (50)     | (50)      | (50)     | (50)     |
| Angiectasis                           |          | 1 [3.0]   | 3 [2.7]  | 1 [3.0]  |
| Cyst                                  | 7 [2.6]  | 10 [2.2]  | 19 [1.9] | 13 [2.2] |
| Hemorrhage                            |          |           | 1 [2.0]  |          |
| Inflammation, Granulomatous           |          | 1 [2.0]   |          |          |
| Mineralization                        |          | 1 [3.0]   |          |          |
| Pigmentation                          |          | 1 [2.0]   |          |          |
| Thrombosis                            | 1 [3.0]  | 1 [3.0]   | 2 [3.0]  |          |
| Periovarian Tissue, Necrosis          | 1 [3.0]  |           |          |          |
| Uterus                                | (50)     | (50)      | (50)     | (50)     |
| Angiectasis                           | 2 [2.0]  | 1 [3.0]   |          |          |
| Inflammation, Suppurative             |          |           |          | 1 [4.0]  |
| Thrombosis                            |          |           | 1 [2.0]  |          |
| Endometrium, Hyperplasia, Cystic      | 50 [3.1] | 49 [2.7]  | 48 [2.7] | 48 [2.9] |
| Vagina                                | (0)      | (0)       | (3)      | (0)      |
| <b>HEMATOPOIETIC SYSTEM</b>           |          |           |          |          |
| Bone Marrow                           | (50)     | (50)      | (50)     | (50)     |
| Angiectasis                           |          | 1 [1.0]   | 1 [3.0]  |          |
| Atrophy, Focal                        | 3 [2.0]  |           | 1 [2.0]  | 2 [2.0]  |
| Myelofibrosis                         | 27 [1.3] | 29 [1.4]  | 27 [1.3] | 27 [1.4] |
| Myeloid Cell, Hyperplasia             | 2 [3.0]  |           |          | 4 [2.0]  |
| Lymph Node                            | (8)      | (6)       | (6)      | (4)      |
| Hyperplasia, Plasma Cell              |          |           |          | 1 [3.0]  |
| Iliac, Ectasia                        |          |           | 1 [2.0]  |          |
| Inguinal, Ectasia                     |          | 1 [2.0]   |          |          |
| Lumbar, Congestion                    |          |           |          | 1 [2.0]  |
| Lumbar, Ectasia                       |          | 2 [3.0]   | 2 [3.0]  |          |
| Lumbar, Hyperplasia, Histiocytic      |          |           |          | 1 [2.0]  |
| Mediastinal, Congestion               |          |           |          | 1 [3.0]  |
| Mediastinal, Hyperplasia, Histiocytic |          |           |          | 1 [2.0]  |
| Renal, Ectasia                        | 2 [3.0]  |           | 1 [3.0]  |          |
| Lymph Node, Mandibular                | (50)     | (50)      | (50)     | (50)     |
| Atrophy                               |          |           | 1 [3.0]  |          |
| Ectasia                               |          | 1 [2.0]   |          |          |
| Hyperplasia, Lymphoid                 | 1 [3.0]  | 4 [2.3]   |          | 5 [2.4]  |
| Hyperplasia, Plasma Cell              | 1 [2.0]  |           |          |          |
| Lymph Node, Mesenteric                | (50)     | (50)      | (50)     | (50)     |

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Lab: BAT

| B6C3F1 MICE FEMALE  | 0 MG/KG  | 0.6 MG/KG | 2 MG/KG  | 6 MG/KG  |
|---|----------|-----------|----------|----------|
| Congestion, Chronic   |          |           |          | 1 [3.0]  |
| Hyperplasia, Histiocytic                                      |          |           |          | 1 [2.0]  |
| Hyperplasia, Lymphoid   |          | 3 [2.0]   | 3 [2.7]  | 2 [2.0]  |
| Hyperplasia, Plasma Cell                                      | 1 [2.0]  | 1 [2.0]   | 1 [2.0]  | 2 [2.0]  |
| Inflammation  |          | 1 [3.0]   |          |          |
| Spleen  | (50)     | (50)      | (50)     | (50)     |
| Fibrosis  |          | 1 [3.0]   |          |          |
| Hematopoietic Cell Proliferation                              | 16 [2.4] | 19 [2.2]  | 18 [2.3] | 22 [2.5] |
| Hyperplasia, Lymphoid   | 13 [2.4] | 19 [2.1]  | 19 [2.3] | 16 [2.3] |
| Pigmentation  | 7 [1.0]  | 5 [1.2]   | 8 [1.3]  | 6 [1.2]  |
| Lymphoid Follicle, Atrophy                                    | 1 [2.0]  |           | 4 [2.5]  | 1 [2.0]  |
| Red Pulp, Atrophy   | 1 [2.0]  |           | 4 [2.3]  | 3 [2.0]  |
| Thymus  | (47)     | (47)      | (48)     | (50)     |
| Atrophy   | 11 [2.5] | 11 [2.4]  | 13 [2.8] | 17 [2.8] |
| Hyperplasia, Atypical   |          | 1 [2.0]   |          |          |
| Hyperplasia, Lymphoid   |          | 5 [2.0]   | 7 [2.1]  | 4 [2.3]  |
| <b>INTEGUMENTARY SYSTEM</b>                                   |          |           |          |          |
| Mammary Gland   | (50)     | (49)      | (50)     | (50)     |
| Hyperplasia   |          |           | 1 [1.0]  |          |
| Skin  | (50)     | (50)      | (50)     | (50)     |
| Site Of Application - Dermis,<br>Inflammation, Chronic Active |          | 9 [1.4]   | 30 [1.3] | 28 [1.4] |
| Site Of Application - Epidermis,<br>Hyperplasia               |          | 12 [1.5]  | 37 [1.2] | 49 [1.5] |
| Site Of Application - Epidermis, Ulcer                        |          | 1 [3.0]   | 2 [2.5]  | 3 [3.0]  |
| Subcutaneous Tissue, Inflammation,<br>Granulomatous           |          |           |          | 1 [3.0]  |
| Subcutaneous Tissue, Necrosis, Fatty                          |          |           |          | 1 [3.0]  |
| Subcutaneous Tissue, Pigmentation                             |          |           |          | 1 [1.0]  |
| <b>MUSCULOSKELETAL SYSTEM</b>                                 |          |           |          |          |
| Bone  | (50)     | (50)      | (50)     | (50)     |
| Arthrosis   |          | 1 [3.0]   |          |          |
| Osteopetrosis   |          |           |          | 1 [3.0]  |
| Skeletal Muscle   | (1)      | (1)       | (1)      | (1)      |

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Lab: BAT

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|---|----------|-----------|----------|----------|
| <b>NERVOUS SYSTEM</b>                       |          |           |          |          |
| Brain                                       | (50)     | (50)      | (50)     | (50)     |
| Hemorrhage                                  |          |           |          | 1 [1.0]  |
| Pigmentation                                |          |           | 1 [2.0]  |          |
| Neuron, Necrosis                            |          |           |          | 1 [1.0]  |
| <b>RESPIRATORY SYSTEM</b>                   |          |           |          |          |
| Lung  | (50)     | (50)      | (50)     | (50)     |
| Hemorrhage                                  |          | 2 [3.0]   |          | 2 [3.0]  |
| Inflammation                                | 1 [3.0]  | 1 [1.0]   |          | 3 [2.0]  |
| Pigmentation                                |          |           |          | 1 [1.0]  |
| Alveolar Epithelium, Hyperplasia            | 1 [2.0]  | 1 [2.0]   |          | 2 [2.0]  |
| Alveolus, Infiltration Cellular, Histiocyte | 2 [2.5]  | 1 [2.0]   | 2 [2.0]  | 1 [1.0]  |
| Mediastinum, Inflammation                   |          | 1 [3.0]   |          |          |
| Serosa, Fibrosis                            |          |           | 1 [3.0]  |          |
| Nose  | (50)     | (50)      | (50)     | (50)     |
| Glands, Cyst                                |          |           |          | 1 [1.0]  |
| Respiratory Epithelium, Inflammation        | 2 [2.0]  |           |          |          |
| Trachea                                     | (50)     | (50)      | (50)     | (50)     |
| <b>SPECIAL SENSES SYSTEM</b>                |          |           |          |          |
| Eye   | (50)     | (50)      | (50)     | (50)     |
| Cornea, Inflammation, Suppurative           |          | 1 [3.0]   |          |          |
| Lens, Degeneration                          | 2 [3.0]  | 2 [2.5]   |          |          |
| Optic Nerve, Degeneration                   |          |           | 1 [2.0]  |          |
| Harderian Gland                             | (50)     | (50)      | (50)     | (50)     |
| Infiltration Cellular, Mononuclear Cell     | 31 [1.1] | 33 [1.1]  | 36 [1.2] | 36 [1.1] |
| Epithelium, Hyperplasia                     | 1 [2.0]  | 1 [3.0]   | 4 [1.0]  | 3 [1.7]  |
| <b>URINARY SYSTEM</b>                       |          |           |          |          |
| Kidney                                      | (50)     | (50)      | (50)     | (50)     |
| Accumulation, Hyaline Droplet               |          | 1 [4.0]   |          |          |
| Amyloid Deposition                          | 2 [2.5]  |           | 1 [3.0]  |          |
| Cyst  |          |           | 1 [1.0]  |          |

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Lab: BAT

| B6C3F1 MICE FEMALE                      | 0 MG/KG  | 0.6 MG/KG | 2 MG/KG  | 6 MG/KG  |
|---|----------|-----------|----------|----------|
| Degeneration                            |          |           |          | 1 [2.0]  |
| Infarct                                 | 3 [2.3]  | 2 [2.5]   | 8 [1.8]  | 4 [2.0]  |
| Inflammation                            | 2 [2.0]  |           |          |          |
| Metaplasia, Osseous                     |          | 1 [2.0]   |          | 1 [2.0]  |
| Mineralization                          | 14 [1.2] | 8 [1.0]   | 4 [1.0]  | 3 [1.0]  |
| Nephropathy                             | 16 [1.3] | 15 [1.0]  | 16 [1.3] | 18 [1.1] |
| Pigmentation                            |          |           | 1 [1.0]  |          |
| Pelvis, Dilatation                      |          |           | 1 [2.0]  |          |
| Renal Tubule, Hyperplasia               | 1 [1.0]  | 2 [1.5]   |          |          |
| Renal Tubule, Necrosis                  | 1 [3.0]  |           |          |          |
| Urinary Bladder                         | (50)     | (50)      | (50)     | (50)     |
| Infiltration Cellular, Mononuclear Cell | 33 [1.8] | 37 [1.3]  | 38 [1.5] | 38 [1.4] |

\*\*\* END OF REPORT \*\*\*