

Chloral Hydrate, NTP TR 503 B-1

TABLE B3

Summary of the Incidence of Nonneoplastic Lesions in Dietary-Controlled Male Mice in the 2-Year Gavage Study of Chloral Hydrate^a

| | Vehicle Control | 25 mg/kg | 50 mg/kg | 100 mg/kg |
|--|-----------------|----------|----------|-----------|
| Disposition Summary | | | | |
| Animals initially in study | 60 | 60 | 60 | 60 |
| 15-Month interim evaluation | | | | |
| Early deaths | | | | |
| Moribund | 1 | 1 | 1 | |
| Natural deaths | 2 | 3 | | 7 |
| Survivors | | | | |
| Terminal sacrifice | 45 | 44 | 47 | 41 |
| Animals examined microscopically | 60 | 60 | 60 | 60 |
| | | | | |
| 15-Month Interim Evaluation | | | | |
| Alimentary System | | | | |
| Liver | (12) | (12) | (12) | (12) |
| Fatty change, peripheral | 1 (8%) | 2 (17%) | 2 (17%) | |
| Granuloma, multiple | | 1 (8%) | | |
| Vacuolization cytoplasmic, centrilobular | 1 (8%) | 2 (17%) | 2 (17%) | |
| | | | | |
| Integumentary System | | | | |
| Skin | | (1) | | |
| Atrophy, focal, hair follicle | | | 1(100%) | |
| | | | | |
| 2-Year Study | | | | |
| Alimentary System | | | | |
| Esophagus | (47) | (4) | (1) | (48) |
| Autolysis | | | | 2 (4%) |
| Gallbladder | (46) | (4) | (1) | (43) |
| Autolysis | | | | 1 (2%) |
| Hemorrhage | | | | 1 (2%) |
| Infiltration cellular, lymphocytic | | | | 1 (2%) |
| Intestine large, cecum | (45) | (4) | (1) | (44) |
| Autolysis | | 1 (25%) | | 2 (5%) |
| Intestine large, colon | (47) | (4) | (1) | (45) |
| Autolysis | | 1 (25%) | | 2 (4%) |
| Intestine large, rectum | (47) | (4) | (1) | (46) |
| Autolysis | | 1 (25%) | | 1 (2%) |
| Intestine small, duodenum | (47) | (4) | (1) | (44) |
| Autolysis | | 1 (25%) | | 2 (5%) |
| Ulcer | | 1 (25%) | | |
| Intestine small, ileum | (48) | (4) | (1) | (44) |
| Autolysis | | 1 (25%) | | 2 (5%) |
| Intestine small, jejunum | (47) | (5) | (1) | (44) |
| Autolysis | | | | 2 (5%) |

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

TABLE B3

Summary of the Incidence of Nonneoplastic Lesions in Dietary-Controlled Male Mice in the 2-Year Gavage Study of Chloral Hydrate

| | Vehicle Control | 25 mg/kg | 50 mg/kg | 100 mg/kg |
|--|-----------------|----------|----------|-----------|
| 2-Year Study (continued) | | | | |
| Alimentary System (continued) | | | | |
| Liver | (48) | (48) | (48) | (48) |
| Autolysis | | | | 1 (2%) |
| Basophilic focus | | 1 (2%) | 2 (4%) | 2 (4%) |
| Clear cell focus | 1 (2%) | 1 (2%) | 2 (4%) | |
| Cyst | | | 1 (2%) | 1 (2%) |
| Eosinophilic focus | | 2 (4%) | | |
| Hyperplasia, focal, ito cell | | | 1 (2%) | |
| Infarct | 1 (2%) | | | |
| Infiltration cellular, lymphocytic | 1 (2%) | 2 (4%) | | |
| Mixed cell focus | 1 (2%) | | | |
| Necrosis, hepatocyte | 1 (2%) | | | 2 (4%) |
| Necrosis, hepatocyte, midzonal | | 1 (2%) | | |
| Thrombus | | | | 1 (2%) |
| Vacuolization cytoplasmic, centrilobular | | 1 (2%) | | |
| Pancreas | (48) | (4) | (1) | (48) |
| Atrophy, acinar cell | 2 (4%) | | | 1 (2%) |
| Autolysis | | | | 2 (4%) |
| Cyst, duct | 1 (2%) | | | |
| Dilatation, duct | 1 (2%) | | | |
| Hyperplasia, lymphoid | 1 (2%) | | | |
| Salivary glands | (48) | (4) | (1) | (48) |
| Atrophy | | | | 1 (2%) |
| Autolysis | | | | 2 (4%) |
| Infiltration cellular, lymphocytic | 5 (10%) | | | 5 (10%) |
| Stomach, forestomach | (47) | (5) | (1) | (47) |
| Autolysis | | | | 1 (2%) |
| Cyst epithelial inclusion | | | | 1 (2%) |
| Hyperplasia, focal | | 1 (20%) | | |
| Metaplasia, squamous | | 1 (20%) | | |
| Stomach, glandular | (47) | (5) | (1) | (47) |
| Autolysis | | 1 (20%) | | 2 (4%) |
| Cyst | 1 (2%) | | | |
| Hyperkeratosis | | | | 1 (2%) |
| Hyperplasia | | | | 1 (2%) |
| Tongue | (48) | (4) | (1) | (48) |
| Autolysis | | | | 2 (4%) |
| Cardiovascular System | | | | |
| Blood vessel | (48) | (4) | (1) | (48) |
| Arteriosclerosis, artery | 2 (4%) | | | |
| Autolysis, aorta | | | | 1 (2%) |
| Mineralization, aorta | 1 (2%) | | | |
| Heart | (48) | (4) | (1) | (48) |
| Autolysis | | | | 1 (2%) |
| Cardiomyopathy | 3 (6%) | | | 2 (4%) |

TABLE B3**Summary of the Incidence of Nonneoplastic Lesions in Dietary-Controlled Male Mice in the 2-Year Gavage Study of Chloral Hydrate**

| | Vehicle Control | 25 mg/kg | 50 mg/kg | 100 mg/kg |
|---|-----------------|----------|----------|-----------|
| 2-Year Study (continued) | | | | |
| Endocrine System | | | | |
| Adrenal gland, cortex | (45) | (4) | (1) | (47) |
| Autolysis | | | | 3 (6%) |
| Cytoplasmic alteration | 1 (2%) | | | 4 (9%) |
| Hyperplasia | 4 (9%) | | | 3 (6%) |
| Hyperplasia, spindle cell | 33 (73%) | | | 24 (51%) |
| Adrenal gland, medulla | (45) | (4) | (1) | (47) |
| Autolysis | | | | 3 (6%) |
| Parathyroid gland | (44) | (3) | (47) | |
| Autolysis | | | | 4 (9%) |
| Cyst | | | | 1 (2%) |
| Thyroid gland | (47) | (4) | (48) | |
| Autolysis | | | | 5 (10%) |
| Cyst, follicle | 3 (6%) | | | 1 (2%) |
| General Body System | | | | |
| None | | | | |
| Genital system | | | | |
| Coagulating gland | (48) | (4) | (1) | (48) |
| Autolysis | | 1 (25%) | | 3 (6%) |
| Epididymis | (48) | (4) | (1) | (48) |
| Autolysis | | 1 (25%) | | 4 (8%) |
| Granuloma sperm | | | | 1 (2%) |
| Inflammation, chronic | | | | 1 (2%) |
| Spermatocele | | | | 1 (2%) |
| Preputial gland | (48) | (4) | (1) | (47) |
| Atrophy | 13 (27%) | 2 (50%) | | 13 (28%) |
| Autolysis | | 1 (25%) | | 3 (6%) |
| Ectasia, duct | 1 (2%) | 1 (25%) | | 1 (2%) |
| Hyperplasia | | | | 1 (2%) |
| Prostate | (47) | (4) | (1) | (46) |
| Atrophy | | | | 1 (2%) |
| Autolysis | | | | 4 (9%) |
| Inflammation, acute | | | | 1 (2%) |
| Seminal vesicle | (48) | (4) | (1) | (48) |
| Autolysis | | 1 (25%) | | 4 (8%) |
| Inflammation, acute | | | | 1 (2%) |
| Testes | (48) | (4) | (1) | (46) |
| Autolysis | | 1 (25%) | | 3 (7%) |
| Degeneration | | | | 1 (2%) |
| Degeneration, unilateral, seminiferous tubule | 1 (2%) | | | |
| Mineralization, unilateral, seminiferous tubule | 1 (2%) | | | |

TABLE B3

Summary of the Incidence of Nonneoplastic Lesions in Dietary-Controlled Male Mice in the 2-Year Gavage Study of Chloral Hydrate

| | Vehicle Control | 25 mg/kg | 50 mg/kg | 100 mg/kg |
|------------------------------------|-----------------|----------|----------|-----------|
| 2-Year Study (continued) | | | | |
| Hematopoietic System | | | | |
| Bone marrow | (48) | (4) | (1) | (48) |
| Autolysis | | | | 1 (2%) |
| Hyperplasia | 1 (2%) | 2 (50%) | | 2 (4%) |
| Lymph node, mandibular | (46) | (3) | (1) | (48) |
| Angiectasis | 1 (2%) | | | |
| Apoptosis, lymphocyte | | 1 (33%) | | |
| Atrophy, lymphocyte | | | | 1 (2%) |
| Autolysis | | | | 2 (4%) |
| Lymph node, mesenteric | (44) | (8) | (3) | (48) |
| Apoptosis, lymphocyte | | 1 (13%) | | |
| Atrophy | 1 (2%) | | | |
| Atrophy, lymphocyte | | | | 1 (2%) |
| Autolysis | | | | 2 (4%) |
| Degeneration | 4 (9%) | 1 (13%) | 1 (33%) | 3 (6%) |
| Hyperplasia | 2 (5%) | | | 3 (6%) |
| Pigmentation | | | | 1 (2%) |
| Spleen | (48) | (8) | (4) | (48) |
| Apoptosis, lymphocyte | | 1 (13%) | | |
| Atrophy, lymphocyte | 1 (2%) | | | 2 (4%) |
| Autolysis | | | | 2 (4%) |
| Hematopoietic cell proliferation | 2 (4%) | 4 (50%) | 1 (25%) | 6 (13%) |
| Hyperplasia, lymphoid | 2 (4%) | | | 1 (2%) |
| Thymus | (39) | (2) | (1) | (30) |
| Apoptosis | | | 1 (100%) | |
| Autolysis | | | | 1 (3%) |
| Cyst | | | | 1 (3%) |
| Integumentary System | | | | |
| Mammary gland | | | (2) | |
| Autolysis | | | | 1 (50%) |
| Skin | (48) | (4) | (1) | (48) |
| Autolysis | | | | 1 (2%) |
| Musculoskeletal System | | | | |
| Bone, femur | (48) | (4) | (1) | (48) |
| Autolysis | | | | 1 (2%) |
| Fibrous osteodystrophy | | | | 1 (2%) |
| Bone, sternum | (48) | (4) | (1) | (48) |
| Autolysis | | | | 1 (2%) |
| Fibrous osteodystrophy | 2 (4%) | | | 2 (4%) |
| Osteopetrosis | 1 (2%) | | | |
| Skeletal muscle | (48) | (4) | (1) | (48) |
| Autolysis | | | | 2 (4%) |
| Infiltration cellular, lymphocytic | | | | 1 (2%) |
| Polyarteritis | | | | 1 (2%) |

TABLE B3

Summary of the Incidence of Nonneoplastic Lesions in Dietary-Controlled Male Mice in the 2-Year Gavage Study of Chloral Hydrate

| | Vehicle Control | 25 mg/kg | 50 mg/kg | 100 mg/kg |
|---|-----------------|----------|----------|-----------|
| 2-Year Study (continued) | | | | |
| Nervous System | | | | |
| Brain, cerebellum | (48) | (4) | (1) | (48) |
| Autolysis | | | | 1 (2%) |
| Brain, cerebrum | (48) | (4) | (1) | (47) |
| Hydrocephalus | | 1 (25%) | | |
| Infiltration cellular, lymphocytic, lateral ventricle | 1 (2%) | | | |
| Mineralization, thalamus | 19 (40%) | 2 (50%) | | 19 (40%) |
| Peripheral nerve | (48) | (4) | (1) | (47) |
| Autolysis | | | | 2 (4%) |
| Degeneration | | | | 1 (2%) |
| Spinal cord | (48) | (3) | (1) | (48) |
| Autolysis | | | | 1 (2%) |
| Respiratory System | | | | |
| Larynx | (46) | (4) | (1) | (48) |
| Autolysis | | | | 2 (2%) |
| Lung | (48) | (6) | (5) | (48) |
| Atelectasis | 1 (2%) | | | |
| Autolysis | | | | 1 (2%) |
| Granuloma, focal | 1 (2%) | | | |
| Hemorrhage, focal, right, apical lobe, sub pleura | | | 1 (20%) | |
| Hemorrhage | 1 (2%) | | | |
| Hyperplasia, alveolar epithelium | 1 (2%) | | | 5 (10%) |
| Infiltration cellular, lymphocytic | 3 (6%) | | | 2 (4%) |
| Nose | (48) | (4) | (1) | (48) |
| Autolysis | | | | 1 (2%) |
| Granuloma | | | | 1 (2%) |
| Trachea | (47) | (4) | (1) | (48) |
| Autolysis | | | | 2 (4%) |
| Special Senses System | | | | |
| Eye | (48) | (4) | (1) | (47) |
| Autolysis | | | | 1 (2%) |
| Harderian gland | (48) | (8) | (2) | (48) |
| Autolysis | | | | 3 (6%) |
| Hyperplasia, unilateral | 1 (2%) | | | 2 (4%) |
| Infiltration cellular, lymphocytic | | | | 2 (4%) |
| Lacrimal gland | (47) | (4) | (1) | (46) |
| Atrophy, focal | | | | 1 (2%) |
| Autolysis | | | | 2 (4%) |
| Infiltration cellular, lymphocytic | 1 (2%) | | | |
| Zymbal's gland | (47) | (3) | (1) | (47) |
| Autolysis | | | | 2 (4%) |

TABLE B3

Summary of the Incidence of Nonneoplastic Lesions in Dietary-Controlled Male Mice in the 2-Year Gavage Study of Chloral Hydrate

| | Vehicle Control | 25 mg/kg | 50 mg/kg | 100 mg/kg |
|--|-----------------|----------|----------|-----------|
| 2-Year Study (continued) | | | | |
| Urinary System | | | | |
| Kidney | (48) | (4) | (1) | (47) |
| Accumulation hyaline droplet, renal tubule | 1 (2%) | | | 2 (4%) |
| Autolysis | | | | 2 (4%) |
| Cyst, renal tubule | 1 (2%) | | | |
| Degeneration, renal tubule | 1 (2%) | | | 4 (9%) |
| Glomerulosclerosis | 2 (4%) | | | 3 (6%) |
| Hyperplasia, focal, unilateral, renal tubule | 1 (2%) | | | |
| Infarct, unilateral | | 1 (25%) | | |
| Infiltration cellular, lymphocytic | 1 (2%) | | | 1 (2%) |
| Mineralization, renal tubule | 1 (2%) | | | |
| Nephropathy | 1 (2%) | | | |
| Regeneration, renal tubule | 2 (4%) | | | 4 (9%) |
| Urinary bladder | (48) | (4) | (1) | (48) |
| Autolysis | | | | 4 (8%) |
| Infiltration cellular, lymphocytic | 1 (2%) | | | |