

Study Number: R10997

Test Type: RACB

Route: Dosing in Feed

Species/Strain: Rat/Sprague-Dawley

C Number:

Study Gender:

PWG Approval Date

PA10R: Statistical Analysis of Non-Neoplastic Lesions with Litter Incidence

Test Compound: Diisobutyl Phthalate

CAS Number: 84-69-5

R10997

Both

See web page for date of PWG Approval

Date Report Requested: 01/09/2020

Time Report Requested: 07:23:03

Lab: RTI

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PA10R: Statistical Analysis of Non-Neoplastic Lesions with Litter Incidence
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| | F0 Male | | | |
|--|------------------------|------|------|----------|
| | Treatment Groups (ppm) | | | |
| | 0 | 1000 | 5000 | 10000 |
| Disposition Summary | | | | |
| Animals Initially In Study | 23 | 23 | 23 | 23 |
| Early Deaths | | | | |
| Scheduled Deaths | | | | |
| Scheduled sacrifice, terminal (SD 139 - 141) | 23 | 23 | 23 | 23 |
| Number of Animals Examined | 23 | 10 | 6 | 23 |
| ALIMENTARY SYSTEM | | | | |
| LIVER | (23) | (0) | (0) | (23) |
| BILE DUCT; HYPERPLASIA | | | | 1 (4.3%) |
| INFLAMMATION; FOCAL | | | | 3 (13%) |
| HEPATOCTE; NECROSIS | | | | 1 (4.3%) |
| CARDIOVASCULAR SYSTEM | | | | |
| None | | | | |
| ENDOCRINE SYSTEM | | | | |
| ADRENAL GLAND | (23) | (0) | (0) | (23) |
| CORTEX; VACUOLATION; DIFFUSE | | | | 1 (4.3%) |
| CORTEX; VACUOLATION; FOCAL | 2 (8.7%) | | | |
| PITUITARY GLAND | (22) | (0) | (0) | (22) |
| PARS DISTALIS; CYST | | | | 1 (4.5%) |
| RATHKE'S CLEFT; DILATION | | | | 1 (4.5%) |
| GENERAL BODY SYSTEM | | | | |
| FAT | (0) | (0) | (0) | (1) |
| INFLAMMATION, CHRONIC | | | | 1 (100%) |

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| | F0 Male | | | |
|--------------------------------------|------------------------|---------|----------|-----------|
| | Treatment Groups (ppm) | | | |
| | 0 | 1000 | 5000 | 10000 |
| GENITAL SYSTEM | | | | |
| DORSAL PROSTATE | (23) | (0) | (0) | (23) |
| INFLAMMATION, CHRONIC | 1 (4.3%) | | | |
| EPIDIDYMIS | (23) | (0) | (0) | (23) |
| DUCT; EXFOLIATED GERM CELL | 3 (13%) | | | 2 (8.7%) |
| MINERAL | | | | 1 (4.3%) |
| NECROSIS | | | | 1 (4.3%) |
| SPERM GRANULOMA | 2 (8.7%) | | | |
| PREPUTIAL GLAND | (10) | (10) | (4) | (9) |
| INFLAMMATION, CHRONIC | 7 (70%) | 6 (60%) | 2 (50%) | 7 (77.8%) |
| BILATERAL; INFLAMMATION, SUPPURATIVE | 1 (10%) | 2 (20%) | 2 (50%) | 2 (22.2%) |
| INFLAMMATION, SUPPURATIVE | 2 (20%) | 1 (10%) | | |
| TESTIS | (23) | (0) | (0) | (23) |
| GERMINAL EPITHELIUM; DEGENERATION | 4 (17.4%) | | | 5 (21.7%) |
| SEMINIFEROUS TUBULE; MINERAL | | | | 1 (4.3%) |
| SEMINIFEROUS TUBULE; NECROSIS | | | | 1 (4.3%) |
| VENTRAL PROSTATE | (23) | (0) | (0) | (23) |
| INFILTRATION CELLULAR; LYMPHOCYTE | 3 (13%) | | | |
| INFLAMMATION, CHRONIC | 2 (8.7%) | | | 2 (8.7%) |
| INFLAMMATION, CHRONIC-ACTIVE | 1 (4.3%) | | | 1 (4.3%) |
| HEMATOLYMPHOID SYSTEM | | | | |
| THYMUS | (23) | (0) | (0) | (23) |
| HYPERPLASIA; EPITHELIAL | 2 (8.7%) | | | 1 (4.3%) |
| INTEGUMENTARY SYSTEM | | | | |
| SKIN | (0) | (0) | (1) | (1) |
| ULCERATION | | | 1 (100%) | 1 (100%) |

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| | F0 Male | | | |
|---------------------------------|-------------------------------|-------------|-------------|--------------|
| | Treatment Groups (ppm) | | | |
| | 0 | 1000 | 5000 | 10000 |
| MUSCULOSKELETAL SYSTEM | | | | |
| None | | | | |
| NERVOUS SYSTEM | | | | |
| None | | | | |
| RESPIRATORY SYSTEM | | | | |
| None | | | | |
| SPECIAL SENSES SYSTEM | | | | |
| None | | | | |
| URINARY SYSTEM | | | | |
| KIDNEY | (23) | (0) | (0) | (23) |
| CHRONIC PROGRESSIVE NEPHROPATHY | 21 (91.3%) | | | 22 (95.7%) |
| DYSPLASIA | 1 (4.3%) | | | |
| INFARCT | | | | 1 (4.3%) |
| INFLAMMATION; INTERSTITIAL | | | | 1 (4.3%) |
| PAPILLA; MINERAL | 2 (8.7%) | | | |
| PELVIS; MINERAL | | | | 1 (4.3%) |

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 Lab: RTI

| | F0 Female | | | |
|--|------------------------|------|----------|----------|
| | Treatment Groups (ppm) | | | |
| | 0 | 1000 | 5000 | 10000 |
| Disposition Summary | | | | |
| Animals Initially In Study | 23 | 23 | 23 | 23 |
| Early Deaths | | | | |
| Euthanized, moribund | 2 | 2 | 2 | 1 |
| Unscheduled Sacrifice | | | 1 | |
| Scheduled Deaths | | | | |
| Scheduled sacrifice, terminal (SD 176 - 177) | 21 | 21 | 20 | 22 |
| Number of Animals Examined | 23 | 3 | 4 | 23 |
| ALIMENTARY SYSTEM | | | | |
| LIVER | (23) | (0) | (1) | (23) |
| INFLAMMATION; FOCAL | 1 (4.3%) | | 1 (100%) | 1 (4.3%) |
| CARDIOVASCULAR SYSTEM | | | | |
| None | | | | |
| ENDOCRINE SYSTEM | | | | |
| ADRENAL GLAND | (23) | (0) | (0) | (23) |
| NECROSIS | | | | 1 (4.3%) |
| CORTEX; VACUOLATION; FOCAL | 1 (4.3%) | | | 1 (4.3%) |
| THYROID GLAND | (23) | (0) | (0) | (23) |
| C-CELL; HYPERPLASIA | 1 (4.3%) | | | 1 (4.3%) |
| GENERAL BODY SYSTEM | | | | |
| FAT | (1) | (0) | (0) | (0) |
| NECROSIS | 1 (100%) | | | |

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Time Report Requested: 07:23:03

Route: Dosing in Feed

CAS Number: 84-69-5

Lab: RTI

Species/Strain: Rat/Sprague-Dawley

| | F0 Female | | | |
|-----------------------------------|------------------------|------|----------|----------|
| | Treatment Groups (ppm) | | | |
| | 0 | 1000 | 5000 | 10000 |
| GENITAL SYSTEM | | | | |
| CLITORAL GLAND | (1) | (0) | (0) | (1) |
| INFLAMMATION, SUPPURATIVE | 1 (100%) | | | 1 (100%) |
| OVARY | (23) | (0) | (0) | (23) |
| CORPUS LUTEUM; BILATERAL; CYST | | | | 2 (8.7%) |
| CORPUS LUTEUM; CYST | | | | 1 (4.3%) |
| CYST; EPITHELIAL | | | | 1 (4.3%) |
| CYST | 3 (13%) | | | 2 (8.7%) |
| UTERUS | (21) | (0) | (0) | (23) |
| DILATION | 1 (4.8%) | | | 1 (4.3%) |
| ENDOMETRIUM; HYPERPLASIA; CYSTIC | 2 (9.5%) | | | |
| ENDOMETRIUM; METAPLASIA; SQUAMOUS | 1 (4.8%) | | | 1 (4.3%) |
| POLYP; STROMAL | | | | 2 (8.7%) |
| VAGINA | (21) | (0) | (0) | (23) |
| MUCIFICATION | | | | 1 (4.3%) |
| HEMATOLYMPHOID SYSTEM | | | | |
| SPLEEN | (0) | (0) | (2) | (1) |
| EXTRAMEDULLARY HEMATOPOIESIS | | | 2 (100%) | 1 (100%) |
| THYMUS | (23) | (0) | (0) | (23) |
| HYPERPLASIA; EPITHELIAL | 3 (13%) | | | |

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Route: Dosing in Feed

CAS Number: 84-69-5

Lab: RTI

Species/Strain: Rat/Sprague-Dawley

F0 Female

Treatment Groups (ppm)

| | 0 | 1000 | 5000 | 10000 |
|--------------------------------------|------------|-----------|----------|------------|
| INTEGUMENTARY SYSTEM | | | | |
| MAMMARY GLAND | (2) | (3) | (2) | (0) |
| INFLAMMATION, ACUTE | | 1 (33.3%) | | |
| INFLAMMATION, CHRONIC-ACTIVE | | 1 (33.3%) | | |
| SKIN | (1) | (0) | (0) | (0) |
| HAIR FOLLICLE; INFLAMMATION, CHRONIC | 1 (100%) | | | |
| SKIN, ABDOMINAL | (0) | (0) | (0) | (1) |
| ULCERATION | | | | 1 (100%) |
| MUSCULOSKELETAL SYSTEM | | | | |
| None | | | | |
| NERVOUS SYSTEM | | | | |
| None | | | | |
| RESPIRATORY SYSTEM | | | | |
| None | | | | |
| SPECIAL SENSES SYSTEM | | | | |
| None | | | | |
| URINARY SYSTEM | | | | |
| KIDNEY | (23) | (0) | (1) | (23) |
| CHRONIC PROGRESSIVE NEPHROPATHY | 19 (82.6%) | | 1 (100%) | 17 (73.9%) |
| MEDULLA; BILATERAL; CYST | | | | 1 (4.3%) |
| MEDULLA; CYST | | | | 4 (17.4%) |
| CORTICOMEDULLARY JUNCTION; MINERAL | 9 (39.1%) | | 1 (100%) | 6 (26.1%) |
| NEPHROBLASTEMATOSIS | 1 (4.3%) | | | |

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Route: Dosing in Feed

CAS Number: 84-69-5

Lab: RTI

Species/Strain: Rat/Sprague-Dawley

F1 Male : F1c NonParent Males

| | Treatment Groups (ppm) | | | |
|---|------------------------|--------------|--------------|-----------------|
| | 0 | 1000 | 5000 | 10000 |
| Disposition Summary | | | | |
| Animals Initially In Study | 45 | 31 | 39 | 40 |
| Early Deaths | | | | |
| Euthanized, moribund | | | | 1 |
| Scheduled Deaths | | | | |
| Scheduled sacrifice, terminal (PND 90 - 92) | 45 | 31 | 39 | 39 |
| Number of Animals Examined | 45 | 31 | 39 | 40 |
| Total number litters | 17 | 13 | 17 | 16 |
| ALIMENTARY SYSTEM | | | | |
| LIVER | (45) | (1) | (2) | (40) |
| INFLAMMATION; CHRONIC | | 1 (100%) [1] | | 1 (2.5%) [1] |
| INFLAMMATION; FOCAL | 32 (71.1%) [15] | | | 31 (77.5%) [15] |
| HEPATOCYTE; NECROSIS | | | 1 (50%) [1] | |
| POLYARTERITIS NODOSA | | | 1 (50%) [1] | |
| CARDIOVASCULAR SYSTEM | | | | |
| None | | | | |
| ENDOCRINE SYSTEM | | | | |
| ADRENAL GLAND | (45) | (0) | (1) | (40) |
| CORTEX; HYPERPLASIA | | | 1 (100%) [1] | |
| POLYARTERITIS NODOSA | | | 1 (100%) [1] | |
| CORTEX; VACUOLATION; DIFFUSE | | | | 2 (5%) [2] |
| PITUITARY GLAND | (45) | (31) | (39) | (40) |
| PARS DISTALIS; CYST; MULTIPLE | | | 1 (2.6%) [1] | |
| PARS DISTALIS; CYST | 3 (6.7%) [3] | 1 (3.2%) [1] | 2 (5.1%) [2] | 1 (2.5%) [1] |
| PARS INTERMEDIA; CYST | | | | 1 (2.5%) [1] |
| PARS DISTALIS; HYPERTROPHY | | | | 3 (7.5%) [2] |

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Lab: RTI

F1 Male : F1c NonParent Males

Treatment Groups (ppm)

| 0 | 1000 | 5000 | 10000 |
|---|------|------|-------|
|---|------|------|-------|

GENERAL BODY SYSTEM

None

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Lab: RTI

Species/Strain: Rat/Sprague-Dawley

F1 Male : F1c NonParent Males

| | Treatment Groups (ppm) | | | |
|---|------------------------|-----------------|---------------|------------------|
| | 0 | 1000 | 5000 | 10000 |
| GENITAL SYSTEM | | | | |
| COWPERS GLAND | (44) | (31) | (39) | (39) |
| HYPOPLASIA | | | | 1 (2.6%) [1] |
| DORSAL PROSTATE | (45) | (31) | (39) | (38) |
| INFLAMMATION, CHRONIC | 1 (2.2%) [1] | | | |
| EPIDIDYMIS | (45) | (31) | (39) | (40) |
| DUCT; ATROPHY | | | 1 (2.6%) [1] | 3 (7.5%) [2] |
| DUCT; EXFOLIATED GERM CELL | 3 (6.7%) [2] * | | 5 (12.8%) [4] | 8 (20%) [7] |
| HYOSPERMIA | 1 (2.2%) [1] | | 1 (2.6%) [1] | 4 (10%) [3] |
| IMMATURE | | | | 1 (2.5%) [1] |
| SPERM GRANULOMA | | | 1 (2.6%) [1] | |
| LEVATOR ANI PLUS BULBOCAVERNOSUS MUSCLE | (45) | (0) | (2) | (39) |
| HYPOPLASIA | | | | 1 (2.6%) [1] |
| PREPUTIAL GLAND | (2) | (0) | (1) | (1) |
| DUCT; DILATION | | | | 1 (100%) [1] |
| INFLAMMATION, CHRONIC | 1 (50%) [1] | | 1 (100%) [1] | |
| TESTIS | (45) | (31) | (39) | (39) |
| GERMINAL EPITHELIUM; ATROPHY | | | | 1 (2.6%) [1] |
| GERMINAL EPITHELIUM; DEGENERATION | 3 (6.7%) [2] ** | 1 (3.2%) [1] | 8 (20.5%) [6] | 10 (25.6%) [8] * |
| SEMINIFEROUS TUBULE; DYSGENESIS | 1 (2.2%) [1] | | 2 (5.1%) [1] | 2 (5.1%) [2] |
| EDEMA | | | | 2 (5.1%) [1] |
| INTERSTITIAL CELL; HYPERPLASIA; DIFFUSE | | | | 2 (5.1%) [1] |
| INTERSTITIAL CELL; HYPERPLASIA; FOCAL | | | | 2 (5.1%) [2] |
| IMMATURE | | | | 1 (2.6%) [1] |
| VENTRAL PROSTATE | (45) | (31) | (39) | (40) |
| IMMATURE | | | | 1 (2.5%) [1] |
| INFILTRATION CELLULAR; LYMPHOCYTE | 16 (35.6%) [11] | 12 (38.7%) [10] | 6 (15.4%) [5] | 17 (42.5%) [9] |
| BILATERAL; INFLAMMATION, CHRONIC | 14 (31.1%) [8] | 5 (16.1%) [4] | 6 (15.4%) [5] | 13 (32.5%) [7] |

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Lab: RTI

F1 Male : F1c NonParent Males

| | Treatment Groups (ppm) | | | |
|---|------------------------|--------------|---------------|------------------------------|
| | 0 | 1000 | 5000 | 10000 |
| INFLAMMATION, CHRONIC | 2 (4.4%) [2] | 3 (9.7%) [3] | 9 (23.1%) [7] | 3 (7.5%) [3] |
| HEMATOLYMPHOID SYSTEM | | | | |
| SPLEEN | (45) | (0) | (1) | (40) |
| FOLLICLE; ATROPHY; LYMPHOID EXTRAMEDULLARY HEMATOPOIESIS | | | 1 (100%) [1] | 1 (2.5%) [1] |
| THYMUS | (45) | (0) | (0) | (40) |
| HYPERPLASIA; EPITHELIAL NECROSIS; LYMPHOCYTIC | 1 (2.2%) [1] | | | 1 (2.5%) [1] 1 (2.5%) [1] |
| INTEGUMENTARY SYSTEM | | | | |
| DIGIT | (0) | (0) | (0) | (1) |
| HYPOPLASIA | | | | 1 (100%) [1] |
| MUSCULOSKELETAL SYSTEM | | | | |
| None | | | | |
| NERVOUS SYSTEM | | | | |
| None | | | | |
| RESPIRATORY SYSTEM | | | | |
| None | | | | |
| SPECIAL SENSES SYSTEM | | | | |
| None | | | | |

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F1 Male : F1c NonParent Males

| | Treatment Groups (ppm) | | | |
|---------------------------------|------------------------|--------------|---------------|-----------------|
| | 0 | 1000 | 5000 | 10000 |
| URINARY SYSTEM | | | | |
| KIDNEY | (45) | (3) | (3) | (40) |
| CHRONIC PROGRESSIVE NEPHROPATHY | 41 (91.1%) [17] | | 1 (33.3%) [1] | 37 (92.5%) [15] |
| MEDULLA; BILATERAL; CYST | 1 (2.2%) [1] | | | |
| MEDULLA; CYST | | | | 5 (12.5%) [4] |
| PELVIS; DILATION | 3 (6.7%) [2] | 3 (100%) [3] | 3 (100%) [3] | 2 (5%) [2] |
| INFARCT | 1 (2.2%) [1] | | | |
| PAPILLA; MINERAL | | | 1 (33.3%) [1] | 3 (7.5%) [2] |
| NEPHROBLASTEMATOSIS | | | | 1 (2.5%) [1] |
| POLYARTERITIS NODOSA | | | 1 (33.3%) [1] | |

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 Lab: RTI

F1 Female : F1c NonParent Female

| | Treatment Groups (ppm) | | | |
|---|------------------------|--------------|--------------|---------------|
| | 0 | 1000 | 5000 | 10000 |
| Disposition Summary | | | | |
| Animals Initially In Study | 28 | 32 | 40 | 32 |
| Early Deaths | | | | |
| Scheduled Deaths | | | | |
| Scheduled sacrifice, terminal (PND 90 - 92) | 28 | 32 | 40 | 32 |
| Number of Animals Examined | 28 | 5 | 3 | 32 |
| Total number litters | 15 | 4 | 3 | 13 |
| ALIMENTARY SYSTEM | | | | |
| LIVER | (28) | (0) | (1) | (32) |
| HEPATODIAPHRAGMATIC NODULE | | | 1 (100%) [1] | |
| BILE DUCT; HYPERPLASIA | | | | 1 (3.1%) [1] |
| INFLAMMATION; FOCAL | 2 (7.1%) [2] | | | 4 (12.5%) [4] |
| MINERAL; FOCAL | | | | 1 (3.1%) [1] |
| MESENTERY | (2) | (1) | (0) | (0) |
| FAT; NECROSIS | | 1 (100%) [1] | | |
| CARDIOVASCULAR SYSTEM | | | | |
| None | | | | |
| ENDOCRINE SYSTEM | | | | |
| ADRENAL GLAND | (28) | (0) | (1) | (32) |
| POLYARTERITIS NODOSA | | | 1 (100%) [1] | |
| PITUITARY GLAND | (28) | (0) | (0) | (32) |
| PARS DISTALIS; CYST | 2 (7.1%) [2] | | | |
| GENERAL BODY SYSTEM | | | | |
| None | | | | |

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Lab: RTI

F1 Female : F1c NonParent Female

| | Treatment Groups (ppm) | | | |
|----------------------------------|------------------------|--------------|--------------|---------------|
| | 0 | 1000 | 5000 | 10000 |
| GENITAL SYSTEM | | | | |
| OVARY | (28) | (0) | (0) | (32) |
| CORPUS LUTEUM; CYST | 1 (3.6%) [1] | | | |
| INTERSTITIAL CELL; HYPERPLASIA | | | | 1 (3.1%) [1] |
| UTERUS | (28) | (1) | (0) | (32) |
| CERVIX; CYST; SQUAMOUS | 1 (3.6%) [1] | | | |
| CYST | | 1 (100%) [1] | | |
| DILATION | 2 (7.1%) [2] | | | 2 (6.3%) [2] |
| ENDOMETRIUM; HYPERPLASIA; CYSTIC | | | | 2 (6.3%) [2] |
| HEMATOLYMPHOID SYSTEM | | | | |
| SPLEEN | (28) | (0) | (1) | (32) |
| EXTRAMEDULLARY HEMATOPOIESIS | | | 1 (100%) [1] | |
| THYMUS | (28) | (0) | (0) | (32) |
| HYPERPLASIA; EPITHELIAL | 1 (3.6%) [1] | | | 1 (3.1%) [1] |
| INTEGUMENTARY SYSTEM | | | | |
| DIGIT | (0) | (1) | (0) | (1) |
| DEVELOPMENTAL MALFORMATION | | 1 (100%) [1] | | 1 (100%) [1] |
| MAMMARY GLAND | (28) | (0) | (0) | (32) |
| ACINUS; HYPERPLASIA | 3 (10.7%) [3] | | | 5 (15.6%) [4] |
| MUSCULOSKELETAL SYSTEM | | | | |
| None | | | | |
| NERVOUS SYSTEM | | | | |
| None | | | | |
| RESPIRATORY SYSTEM | | | | |
| None | | | | |

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Lab: RTI

F1 Male : F1c Parental Males

| | Treatment Groups (ppm) | | | |
|---|------------------------|------|------|---------------|
| | 0 | 1000 | 5000 | 10000 |
| Disposition Summary | | | | |
| Animals Initially In Study | 40 | 40 | 40 | 40 |
| Early Deaths | | | | |
| Unscheduled Sacrifice | | | 3 | |
| Scheduled Deaths | | | | |
| Scheduled sacrifice, terminal (PND 213 - 223) | 40 | 40 | 37 | 40 |
| Number of Animals Examined | 40 | 40 | 40 | 40 |
| Total number litters | 21 | 20 | 19 | 18 |
| ALIMENTARY SYSTEM | | | | |
| LIVER | (40) | (0) | (3) | (40) |
| BILE DUCT; HYPERPLASIA | | | | 1 (2.5%) [1] |
| INFLAMMATION; FOCAL | 5 (12.5%) [5] | | | 5 (12.5%) [4] |
| HEPATOCYTE; NECROSIS | | | | 1 (2.5%) [1] |
| CARDIOVASCULAR SYSTEM | | | | |
| None | | | | |

Study Number: R10997

PA10R: Statistical Analysis of Non-Neoplastic Lesions with Litter Incidence

Date Report Requested: 01/09/2020

Test Type: RACB

Test Compound: Diisobutyl Phthalate

Time Report Requested: 07:23:03

Route: Dosing in Feed

CAS Number: 84-69-5

Lab: RTI

Species/Strain: Rat/Sprague-Dawley

F1 Male : F1c Parental Males

| | Treatment Groups (ppm) | | | |
|--------------------------------|------------------------|------------|--------------|--------------|
| | 0 | 1000 | 5000 | 10000 |
| ENDOCRINE SYSTEM | | | | |
| ADRENAL GLAND | (40) | (0) | (3) | (40) |
| CORTEX; HYPERTROPHY; FOCAL | 2 (5%) [2] | | | |
| CORTEX; VACUOLATION; DIFFUSE | 2 (5%) [2] | | | 3 (7.5%) [3] |
| CORTEX; VACUOLATION; FOCAL | 3 (7.5%) [3] | | | 1 (2.5%) [1] |
| PITUITARY GLAND | (40) | (40) | (40) | (40) |
| PARS DISTALIS; CYST | 4 (10%) [4] | 2 (5%) [2] | 2 (5%) [2] | |
| PARS INTERMEDIA; CYST | 1 (2.5%) [1] | | | |
| PARS DISTALIS; HYPERPLASIA | | | | 1 (2.5%) [1] |
| PARS DISTALIS; HYPERTROPHY | 0 * | | 1 (2.5%) [1] | 4 (10%) [3] |
| THYROID GLAND | (40) | (0) | (3) | (40) |
| INFILTRATION; MONONUCLEAR CELL | 1 (2.5%) [1] | | | |
| GENERAL BODY SYSTEM | | | | |
| None | | | | |

Study Number: R10997

PA10R: Statistical Analysis of Non-Neoplastic Lesions with Litter Incidence

Date Report Requested: 01/09/2020

Test Type: RACB

Test Compound: Diisobutyl Phthalate

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Route: Dosing in Feed

CAS Number: 84-69-5

Lab: RTI

Species/Strain: Rat/Sprague-Dawley

F1 Male : F1c Parental Males

| | Treatment Groups (ppm) | | | |
|---|------------------------|--------------|---------------|--------------------|
| | 0 | 1000 | 5000 | 10000 |
| GENITAL SYSTEM | | | | |
| COWPERS GLAND | (40) | (40) | (40) | (40) |
| HYPOPLASIA | | | | 1 (2.5%) [1] |
| DORSAL PROSTATE | (40) | (0) | (3) | (40) |
| INFLAMMATION, ACUTE | | | 1 (33.3%) [1] | 1 (2.5%) [1] |
| EPIDIDYMIS | (40) | (40) | (40) | (39) |
| DUCT; ATROPHY | 0 ** | | 2 (5%) [2] | 5 (12.8%) [5] |
| DUCT; EXFOLIATED GERM CELL | 2 (5%) [2] * | 1 (2.5%) [1] | 3 (7.5%) [3] | 6 (15.4%) [5] |
| HYPOPLASIA | 0 * | | 1 (2.5%) [1] | 3 (7.7%) [3] |
| HYOSPERMIA | 0 ** | | 3 (7.5%) [3] | 8 (20.5%) [6] * |
| PREPUTIAL GLAND | (2) | (1) | (2) | (8) |
| DUCT; DILATION | | | | 2 (25%) [2] |
| BILATERAL; INFLAMMATION, CHRONIC | 1 (50%) [1] | | | |
| INFLAMMATION, CHRONIC | 1 (50%) [1] | | | |
| BILATERAL; INFLAMMATION, SUPPURATIVE | | | 1 (50%) [1] | 2 (25%) [2] |
| INFLAMMATION, SUPPURATIVE | | 1 (100%) [1] | 1 (50%) [1] | 4 (50%) [3] |
| SEMINAL VESICLE | (40) | (0) | (3) | (40) |
| INFLAMMATION; ACUTE | | | | 1 (2.5%) [1] |
| TESTIS | (40) | (40) | (40) | (39) |
| GERMINAL EPITHELIUM; ATROPHY | 0 ** | | | 5 (12.8%) [5] |
| GERMINAL EPITHELIUM; DEGENERATION | 2 (5%) [2] ** | 3 (7.5%) [3] | 7 (17.5%) [6] | 13 (33.3%) [10] ** |
| SEMINIFEROUS TUBULE; DYSGENESIS | | 1 (2.5%) [1] | 1 (2.5%) [1] | 1 (2.6%) [1] |
| EDEMA | 0 * | | 1 (2.5%) [1] | 4 (10.3%) [4] |
| INTERSTITIAL CELL; HYPERPLASIA; DIFFUSE | 0 * | | 1 (2.5%) [1] | 4 (10.3%) [4] |
| INTERSTITIAL CELL; HYPERPLASIA; FOCAL | 0 * | | | 4 (10.3%) [4] |
| HYPOPLASIA | | | 1 (2.5%) [1] | 2 (5.1%) [2] |
| MINERAL | | | 1 (2.5%) [1] | |
| VENTRAL PROSTATE | (40) | (40) | (40) | (40) |

Study Number: R10997
Test Type: RACB
Route: Dosing in Feed
Species/Strain: Rat/Sprague-Dawley

PA10R: Statistical Analysis of Non-Neoplastic Lesions with Litter Incidence
Test Compound: Diisobutyl Phthalate
CAS Number: 84-69-5

Date Report Requested: 01/09/2020
Time Report Requested: 07:23:03
Lab: RTI

F1 Male : F1c Parental Males

| | Treatment Groups (ppm) | | | |
|--|-------------------------------|---------------|-------------|-----------------------------|
| | 0 | 1000 | 5000 | 10000 |
| INFILTRATION CELLULAR; LYMPHOCYTE INFLAMMATION, CHRONIC | 5 (12.5%) [5] 1 (2.5%) [1] | 5 (12.5%) [5] | 4 (10%) [4] | 8 (20%) [7] 3 (7.5%) [3] |
| HEMATOLYMPHOID SYSTEM | | | | |
| LYMPH NODE | (0) | (0) | (0) | (1) |
| HYPERPLASIA; PLASMA CELL | | | | 1 (100%) [1] |
| THYMUS | (40) | (0) | (3) | (39) |
| ATROPHY | 1 (2.5%) [1] | | | |
| HYPERPLASIA; EPITHELIAL | 7 (17.5%) [6] | | | 3 (7.7%) [3] |
| INTEGUMENTARY SYSTEM | | | | |
| SKIN | (0) | (0) | (0) | (1) |
| INFLAMMATION, SUPPURATIVE | | | | 1 (100%) [1] |
| MUSCULOSKELETAL SYSTEM | | | | |
| None | | | | |
| NERVOUS SYSTEM | | | | |
| None | | | | |
| RESPIRATORY SYSTEM | | | | |
| None | | | | |
| SPECIAL SENSES SYSTEM | | | | |
| None | | | | |

Study Number: R10997

Test Type: RACB

Route: Dosing in Feed

Species/Strain: Rat/Sprague-Dawley

PA10R: Statistical Analysis of Non-Neoplastic Lesions with Litter Incidence

Test Compound: Diisobutyl Phthalate

CAS Number: 84-69-5

Date Report Requested: 01/09/2020

Time Report Requested: 07:23:03

Lab: RTI

F1 Male : F1c Parental Males

| | Treatment Groups (ppm) | | | |
|------------------------------------|------------------------|--------------|--------------|----------------|
| | 0 | 1000 | 5000 | 10000 |
| URINARY SYSTEM | | | | |
| KIDNEY | (40) | (1) | (3) | (40) |
| PELVIS; CALCULUS | 6 (15%) [5] | | | |
| CHRONIC PROGRESSIVE NEPHROPATHY | 39 (97.5%) [21] | 1 (100%) [1] | 3 (100%) [3] | 40 (100%) [18] |
| MEDULLA; CYST | 1 (2.5%) [1] | | | |
| PELVIS; DILATION | 2 (5%) [2] | 1 (100%) [1] | | 3 (7.5%) [3] |
| CORTICOMEDULLARY JUNCTION; MINERAL | | | | 1 (2.5%) [1] |
| PAPILLA; MINERAL | 1 (2.5%) [1] | | | 5 (12.5%) [4] |
| PELVIS; MINERAL | 1 (2.5%) [1] | | | |

Study Number: R10997
 Test Type: RACB
 Route: Dosing in Feed
 Species/Strain: Rat/Sprague-Dawley

PA10R: Statistical Analysis of Non-Neoplastic Lesions with Litter Incidence
 Test Compound: Diisobutyl Phthalate
 CAS Number: 84-69-5

Date Report Requested: 01/09/2020
 Time Report Requested: 07:23:03
 Lab: RTI

F1 Female : F1c Parental Females

| | Treatment Groups (ppm) | | | |
|--|------------------------|--------------|---------------|--------------|
| | 0 | 1000 | 5000 | 10000 |
| Disposition Summary | | | | |
| Animals Initially In Study | 40 | 40 | 40 | 40 |
| Early Deaths | | | | |
| Euthanized, moribund | 1 | | 4 | |
| Found Dead | 1 | | 1 | |
| Scheduled Deaths | | | | |
| Scheduled sacrifice, terminal (LD 21, PND 232 - 237) | 38 | 40 | 35 | 40 |
| Number of Animals Examined | 40 | 7 | 9 | 40 |
| Total number litters | 20 | 7 | 9 | 18 |
| ALIMENTARY SYSTEM | | | | |
| LIVER | (40) | (2) | (6) | (40) |
| HEPATODIAPHRAGMATIC NODULE | | 1 (50%) [1] | 1 (16.7%) [1] | |
| BILE DUCT; HYPERPLASIA | | | | 1 (2.5%) [1] |
| INFLAMMATION; FOCAL | 2 (5%) [2] | | 1 (16.7%) [1] | |
| HEPATOCYTE; NECROSIS | | 1 (50%) [1] | 1 (16.7%) [1] | |
| MESENTERY | (0) | (1) | (1) | (0) |
| FAT; NECROSIS | | 1 (100%) [1] | | |
| PERIARTERITIS | | | 1 (100%) [1] | |
| CARDIOVASCULAR SYSTEM | | | | |
| HEART | (0) | (0) | (1) | (0) |
| CARDIOMYOPATHY | | | 1 (100%) [1] | |
| POLYARTERITIS NODOSA | | | 1 (100%) [1] | |

Study Number: R10997

PA10R: Statistical Analysis of Non-Neoplastic Lesions with Litter Incidence

Date Report Requested: 01/09/2020

Test Type: RACB

Test Compound: Diisobutyl Phthalate

Time Report Requested: 07:23:03

Route: Dosing in Feed

CAS Number: 84-69-5

Lab: RTI

Species/Strain: Rat/Sprague-Dawley

F1 Female : F1c Parental Females

Treatment Groups (ppm)

| | 0 | 1000 | 5000 | 10000 |
|-------------------------|--------------|------|-------------|--------------|
| ENDOCRINE SYSTEM | | | | |
| ADRENAL GLAND | (40) | (0) | (5) | (40) |
| CORTEX; HEMORRHAGE | | | 1 (20%) [1] | |
| CORTEX; HYPERPLASIA | | | 1 (20%) [1] | |
| PITUITARY GLAND | (40) | (0) | (5) | (40) |
| PARS DISTALIS; CYST | 3 (7.5%) [2] | | | 2 (5%) [2] |
| THYROID GLAND | (40) | (0) | (5) | (40) |
| FOLLICLE; CYST | | | | 1 (2.5%) [1] |
| C-CELL; HYPERPLASIA | 1 (2.5%) [1] | | | |

GENERAL BODY SYSTEM

None

Study Number: R10997

PA10R: Statistical Analysis of Non-Neoplastic Lesions with Litter Incidence

Date Report Requested: 01/09/2020

Test Type: RACB

Test Compound: Diisobutyl Phthalate

Time Report Requested: 07:23:03

Route: Dosing in Feed

CAS Number: 84-69-5

Lab: RTI

Species/Strain: Rat/Sprague-Dawley

F1 Female : F1c Parental Females

| | Treatment Groups (ppm) | | | |
|--|------------------------|--------------|--------------|--------------|
| | 0 | 1000 | 5000 | 10000 |
| GENITAL SYSTEM | | | | |
| CERVIX | (40) | (0) | (5) | (40) |
| INFLAMMATION; ACUTE | | | 1 (20%) [1] | |
| POLYARTERITIS NODOSA | | | 1 (20%) [1] | |
| CLITORAL GLAND | (3) | (1) | (1) | (0) |
| DUCT; DILATION | 1 (33.3%) [1] | | | |
| INFLAMMATION, SUPPURATIVE | | 1 (100%) [1] | 1 (100%) [1] | |
| OVARY | (40) | (0) | (5) | (40) |
| CORPUS LUTEUM; BILATERAL; CYST | 2 (5%) [2] | | | 1 (2.5%) [1] |
| CORPUS LUTEUM; CYST | 4 (10%) [4] | | | |
| CYST | 1 (2.5%) [1] | | | 1 (2.5%) [1] |
| POLYARTERITIS NODOSA | | | 1 (20%) [1] | |
| UTERUS | (39) | (1) | (5) | (40) |
| CERVIX; CYST; SQUAMOUS | 1 (2.6%) [1] | | | |
| ENDOMETRIUM; CYST | 2 (5.1%) [1] | | | |
| SUBSEROA; CYST | | 1 (100%) [1] | | |
| ENDOMETRIUM; DILATION; GLANDULAR, CYSTIC | | | | 2 (5%) [1] |
| DILATION | 1 (2.6%) [1] | | | |
| INFLAMMATION; ACUTE | | | 2 (40%) [2] | |
| ENDOMETRIUM; METAPLASIA; SQUAMOUS | 1 (2.6%) [1] | | | |
| POLYARTERITIS NODOSA | | | 1 (20%) [1] | |
| POLYP; STROMAL | 1 (2.6%) [1] | | | |
| VAGINA | (40) | (0) | (5) | (40) |
| CYST; SQUAMOUS | 1 (2.5%) [1] | | | |
| INFLAMMATION; ACUTE | | | 1 (20%) [1] | 1 (2.5%) [1] |
| MUCIFICATION | | | 1 (20%) [1] | |
| POLYARTERITIS NODOSA | | | 1 (20%) [1] | |

Study Number: R10997

Test Type: RACB

Route: Dosing in Feed

Species/Strain: Rat/Sprague-Dawley

PA10R: Statistical Analysis of Non-Neoplastic Lesions with Litter Incidence

Test Compound: Diisobutyl Phthalate

CAS Number: 84-69-5

Date Report Requested: 01/09/2020

Time Report Requested: 07:23:03

Lab: RTI

F1 Female : F1c Parental Females

| | Treatment Groups (ppm) | | | |
|-------------------------------|------------------------|------|---------------|---------------|
| | 0 | 1000 | 5000 | 10000 |
| HEMATOLYMPHOID SYSTEM | | | | |
| LYMPH NODE, AXILLARY | (1) | (0) | (1) | (0) |
| HYPERPLASIA; LYMPHOCYTE | | | 1 (100%) [1] | |
| HYPERPLASIA; PLASMA CELL | 1 (100%) [1] | | | |
| LYMPH NODE, MANDIBULAR | (0) | (0) | (1) | (0) |
| HYPERPLASIA; LYMPHOID | | | 1 (100%) [1] | |
| SPLEEN | (40) | (0) | (5) | (40) |
| EXTRAMEDULLARY HEMATOPOIESIS | 1 (2.5%) [1] | | 5 (100%) [5] | |
| THYMUS | (39) | (0) | (4) | (40) |
| ATROPHY | 10 (25.6%) [8] | | | 12 (30%) [11] |
| CYST | 1 (2.6%) [1] | | | |
| HYPERPLASIA; EPITHELIAL | 3 (7.7%) [3] | | | 4 (10%) [4] |
| INTEGUMENTARY SYSTEM | | | | |
| MAMMARY GLAND | (38) | (2) | (6) | (40) |
| INFLAMMATION; ACUTE | | | 1 (16.7%) [1] | |
| SKIN | (1) | (0) | (0) | (0) |
| INFLAMMATION, SUPPURATIVE | 1 (100%) [1] | | | |
| SKIN, SUBCUTANEOUS TISSUE | (0) | (0) | (1) | (0) |
| INFLAMMATION, SUPPURATIVE | | | 1 (100%) [1] | |
| MUSCULOSKELETAL SYSTEM | | | | |
| None | | | | |
| NERVOUS SYSTEM | | | | |
| None | | | | |
| RESPIRATORY SYSTEM | | | | |
| None | | | | |

Study Number: R10997
Test Type: RACB
Route: Dosing in Feed
Species/Strain: Rat/Sprague-Dawley

PA10R: Statistical Analysis of Non-Neoplastic Lesions with Litter Incidence
Test Compound: Diisobutyl Phthalate
CAS Number: 84-69-5

Date Report Requested: 01/09/2020
Time Report Requested: 07:23:03
Lab: RTI

F1 Female : F1c Parental Females

| | Treatment Groups (ppm) | | | |
|------------------------------------|-------------------------------|-------------|---------------|--------------------|
| | 0 | 1000 | 5000 | 10000 |
| SPECIAL SENSES SYSTEM | | | | |
| None | | | | |
| URINARY SYSTEM | | | | |
| KIDNEY | (40) | (0) | (6) | (40) |
| CHRONIC PROGRESSIVE NEPHROPATHY | 30 (75%) [17] | | 6 (100%) [6] | 34 (85%) [17] |
| MEDULLA; CYST | 1 (2.5%) [1] | | | |
| PAPILLA; DILATION; TUBULAR | | | | 1 (2.5%) [1] |
| PELVIS; DILATION | | | 1 (16.7%) [1] | |
| CORTICOMEDULLARY JUNCTION; MINERAL | 33 (82.5%) [18] | | 3 (50%) [3] | 13 (32.5%) [11] ** |
| PAPILLA; MINERAL | 2 (5%) [2] | | | 3 (7.5%) [3] |
| NEPHROBLASTEMATOSIS | | | | 1 (2.5%) [1] |
| POLYARTERITIS NODOSA | | | 1 (16.7%) [1] | |

Study Number: R10997
Test Type: RACB
Route: Dosing in Feed
Species/Strain: Rat/Sprague-Dawley

PA10R: Statistical Analysis of Non-Neoplastic Lesions with Litter Incidence
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LEGEND

Number of animals examined for each tissue shown in parentheses. If none of the animals examined have the specific lesion then there is a blank for that dose group for that specific lesion. The exception to this is if statistical significance is found for a lesion and the control group has no animals with the lesion then a 0 is included for the control group on the table for that lesion.

Number of animals with observation reported with percent incidence in parentheses

Number of litters with observations shown in square brackets for F1 and F2 animals. F1 litter incidence based on the number of F0 dams; F2 litter incidence based on number of F1 dams.

Trend significance is reported only for those organs that were fully examined in the control group plus two or more other dose groups. For organs that were fully examined in just the control and one other dose group, only the pairwise significance is reported.

All trend and pairwise p-values are reported as one-sided.

Statistical significance for the control group indicates a significant trend test

Statistical significance for a treatment group indicates a significant pairwise test compared to the vehicle control group

Non-pregnant females from the F0 and F1 generations are included in the analysis.

Statistical analysis for the F0 animals was performed by Cochran-Armitage test with poly-3 adjustment for both trend and pairwise tests.

Statistical analysis for the F1 Non-parental and F2 animals was performed by Cochran-Armitage test with a Rao-Scott modification for the random effect due to litter.

Statistical analysis for the F1 Parental animals was performed by Cochran-Armitage test with a poly-3 adjustment for age and a Rao-Scott modification for the random effect due to litter.

* Statistically significant at $P \leq 0.05$

** Statistically significant at $P \leq 0.01$

**** END OF REPORT ****