

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
 TOTAL France S.A.

 TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS
 F2 PUPS

DOSE GROUP : 3, 500mg/kg/d.F2P
 SEX : MALE

| | | | | | |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| ANIMAL NUMBER | : | 9769-02 | 9770-03 | 9771-02 | 9772-02 |
| DAYS ON TEST | : | 22 | 22 | 24 | 22 |
| DATE OF NECROPSY | : | 13-NOV-03 | 14-NOV-03 | 17-NOV-03 | 13-NOV-03 |
| DEFND./ACTUAL NECR.STATE: | | K0/K0 | K0/K0 | K0/K0 | K0/K0 |
| | | | | | |
| FINAL BODY WEIGHT | G: | 46.4910 | 44.8190 | 68.0970 | 53.5900 |
| | | | | | |
| BRAIN | G: | 1.3230 | 1.4350 | 1.6060 | 1.4850 |
| | % BODY : | 2.846 | 3.202 | 2.358 | 2.771 |
| | | | | | |
| SPLEEN | G: | 0.2130 | 0.1800 | 0.3280 | 0.3020 |
| | % BODY : | 0.45815 | 0.40162 | 0.48167 | 0.56354 |
| | % BRAIN: | 16.100 | 12.544 | 20.423 | 20.337 |
| | | | | | |
| THYMUS | G: | 0.1970 | 0.2070 | 0.3190 | 0.2240 |
| | % BODY : | 0.42374 | 0.46186 | 0.46845 | 0.41799 |
| | % BRAIN: | 14.890 | 14.425 | 19.863 | 15.084 |
| | | | | | |

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TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS
F2 PUPS

DOSE GROUP : 3, 500mg/kg/d.F2P
SEX : MALE

ANIMAL NUMBER : 9774-02 9775-02
DAYS ON TEST : 22 22
DATE OF NECROPSY : 14-NOV-03 13-NOV-03
DEFND./ACTUAL NECR.STATE: K0/K0 K0/K0
.....

FINAL BODY WEIGHT G: 54.5670 51.5950
.....

BRAIN G: 1.4320 1.5160
% BODY : 2.624 2.938
.....

SPLEEN G: 0.2540 0.2700
% BODY : 0.46548 0.52331
% BRAIN: 17.737 17.810
.....

THYMUS G: 0.2530 0.2240
% BODY : 0.46365 0.43415
% BRAIN: 17.668 14.776
.....

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 TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS
 F2 PUPS

DOSE GROUP : 3, 500mg/kg/d.F2P
 SEX : FEMALE

| | | | | | |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| ANIMAL NUMBER | : | 9751-08 | 9752-08 | 9753-08 | 9754-11 |
| DAYS ON TEST | : | 24 | 22 | 22 | 24 |
| DATE OF NECROPSY | : | 17-NOV-03 | 14-NOV-03 | 14-NOV-03 | 18-NOV-03 |
| DEFND./ACTUAL NECR.STATE: | | K0/K0 | K0/K0 | K0/K0 | K0/K0 |
| | | | | | |
| FINAL BODY WEIGHT | G: | 64.0910 | 47.3620 | 58.8670 | 69.1360 |
| | | | | | |
| BRAIN | G: | 1.3660 | 1.6300 | 1.3850 | 1.5130 |
| | % BODY : | 2.131 | 3.442 | 2.353 | 2.188 |
| | | | | | |
| SPLEEN | G: | 0.2840 | 0.4210 | 0.2470 | 0.2050 |
| | % BODY : | 0.44312 | 0.88890 | 0.41959 | 0.29652 |
| | % BRAIN: | 20.791 | 25.828 | 17.834 | 13.549 |
| | | | | | |
| THYMUS | G: | 0.2900 | 0.4350 | 0.2190 | 0.2910 |
| | % BODY : | 0.45248 | 0.91846 | 0.37203 | 0.42091 |
| | % BRAIN: | 21.230 | 26.687 | 15.812 | 19.233 |
| | | | | | |

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 F2 PUPS

DOSE GROUP : 3, 500mg/kg/d.F2P
 SEX : FEMALE

| | | | | | |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| ANIMAL NUMBER | : | 9755-07 | 9756-10 | 9757-10 | 9758-10 |
| DAYS ON TEST | : | 22 | 24 | 24 | 24 |
| DATE OF NECROPSY | : | 13-NOV-03 | 17-NOV-03 | 17-NOV-03 | 17-NOV-03 |
| DEFND./ACTUAL NECR.STATE: | | K0/K0 | K0/K0 | K0/K0 | K0/K0 |
| | | | | | |
| FINAL BODY WEIGHT | G: | 41.6710 | 52.5130 | 71.4070 | 73.9320 |
| | | | | | |
| BRAIN | G: | 1.3760 | 1.2380 | 1.5350 | 1.5570 |
| | % BODY : | 3.302 | 2.358 | 2.150 | 2.106 |
| | | | | | |
| SPLEEN | G: | 0.2080 | 0.2510 | 0.2940 | 0.3060 |
| | % BODY : | 0.49915 | 0.47798 | 0.41172 | 0.41389 |
| | % BRAIN: | 15.116 | 20.275 | 19.153 | 19.653 |
| | | | | | |
| THYMUS | G: | 0.1890 | 0.2770 | 0.2900 | 0.3000 |
| | % BODY : | 0.45355 | 0.52749 | 0.40612 | 0.40578 |
| | % BRAIN: | 13.735 | 22.375 | 18.893 | 19.268 |
| | | | | | |

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 F2 PUPS

DOSE GROUP : 3, 500mg/kg/d.F2P
 SEX : FEMALE

| | | | | | |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| ANIMAL NUMBER | : | 9759-09 | 9760-14 | 9763-12 | 9764-09 |
| DAYS ON TEST | : | 24 | 22 | 24 | 24 |
| DATE OF NECROPSY | : | 17-NOV-03 | 13-NOV-03 | 17-NOV-03 | 17-NOV-03 |
| DEFND./ACTUAL NECR.STATE: | | K0/K0 | K0/K0 | K0/K0 | K0/K0 |
| | | | | | |
| FINAL BODY WEIGHT | G: | 61.7540 | 52.2250 | 68.2590 | 71.1350 |
| | | | | | |
| BRAIN | G: | 1.4470 | 1.3520 | 1.5750 | 1.6170 |
| | % BODY : | 2.343 | 2.589 | 2.307 | 2.273 |
| | | | | | |
| SPLEEN | G: | 0.3490 | 0.3090 | 0.3580 | 0.4580 |
| | % BODY : | 0.56515 | 0.59167 | 0.52447 | 0.64385 |
| | % BRAIN: | 24.119 | 22.855 | 22.730 | 28.324 |
| | | | | | |
| THYMUS | G: | 0.2740 | 0.2490 | 0.3350 | 0.2850 |
| | % BODY : | 0.44370 | 0.47678 | 0.49078 | 0.40065 |
| | % BRAIN: | 18.936 | 18.417 | 21.270 | 17.625 |
| | | | | | |

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 F2 PUPS

DOSE GROUP : 3, 500mg/kg/d.F2P
 SEX : FEMALE

| | | | | | |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| ANIMAL NUMBER | : | 9765-06 | 9766-12 | 9767-07 | 9768-06 |
| DAYS ON TEST | : | 22 | 22 | 23 | 22 |
| DATE OF NECROPSY | : | 13-NOV-03 | 12-NOV-03 | 18-NOV-03 | 14-NOV-03 |
| DEFND./ACTUAL NECR.STATE: | | K0/K0 | K0/K0 | K0/K0 | K0/K0 |
| | | | | | |
| FINAL BODY WEIGHT | G: | 57.6720 | 52.4290 | 51.1110 | 52.3360 |
| | | | | | |
| BRAIN | G: | 1.5080 | 1.3620 | 1.3820 | 1.3620 |
| | % BODY : | 2.615 | 2.598 | 2.704 | 2.602 |
| | | | | | |
| SPLEEN | G: | 0.3300 | 0.3040 | 0.2950 | 0.2530 |
| | % BODY : | 0.57220 | 0.57983 | 0.57718 | 0.48341 |
| | % BRAIN: | 21.883 | 22.320 | 21.346 | 18.576 |
| | | | | | |
| THYMUS | G: | 0.2440 | 0.3010 | 0.2420 | 0.2860 |
| | % BODY : | 0.42308 | 0.57411 | 0.47348 | 0.54647 |
| | % BRAIN: | 16.180 | 22.100 | 17.511 | 20.999 |
| | | | | | |

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 F2 PUPS

DOSE GROUP : 3, 500mg/kg/d.F2P
 SEX : FEMALE

| | | | | | |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| ANIMAL NUMBER | : | 9769-07 | 9770-11 | 9771-09 | 9772-09 |
| DAYS ON TEST | : | 22 | 22 | 24 | 22 |
| DATE OF NECROPSY | : | 13-NOV-03 | 14-NOV-03 | 17-NOV-03 | 13-NOV-03 |
| DEFND./ACTUAL NECR.STATE: | | K0/K0 | K0/K0 | K0/K0 | K0/K0 |
| | | | | | |
| FINAL BODY WEIGHT | G: | 48.4380 | 50.0700 | 62.2630 | 55.4580 |
| | | | | | |
| BRAIN | G: | 1.3900 | 1.4520 | 1.5870 | 1.5200 |
| | % BODY : | 2.870 | 2.900 | 2.549 | 2.741 |
| | | | | | |
| SPLEEN | G: | 0.2000 | 0.2320 | 0.3700 | 0.3000 |
| | % BODY : | 0.41290 | 0.46335 | 0.59425 | 0.54095 |
| | % BRAIN: | 14.388 | 15.978 | 23.314 | 19.737 |
| | | | | | |
| THYMUS | G: | 0.2160 | 0.2980 | 0.2920 | 0.2570 |
| | % BODY : | 0.44593 | 0.59517 | 0.46898 | 0.46341 |
| | % BRAIN: | 15.540 | 20.523 | 18.399 | 16.908 |
| | | | | | |

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TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS
F2 PUPS

DOSE GROUP : 3, 500mg/kg/d.F2P
SEX : FEMALE

ANIMAL NUMBER : 9774-03 9775-08
DAYS ON TEST : 22 22
DATE OF NECROPSY : 14-NOV-03 13-NOV-03
DEFND./ACTUAL NECR.STATE: K0/K0 K0/K0
.....

FINAL BODY WEIGHT G: 52.1680 51.0160
.....

BRAIN G: 1.3800 1.4870
% BODY : 2.645 2.915
.....

SPLEEN G: 0.2680 0.2470
% BODY : 0.51372 0.48416
% BRAIN: 19.420 16.611
.....

THYMUS G: 0.1860 0.2610
% BODY : 0.35654 0.51160
% BRAIN: 13.478 17.552
.....

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 TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS
 F2 PUPS

DOSE GROUP : 4, 1000mg/kg/d.F2P
 SEX : MALE

| | | | | | |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| ANIMAL NUMBER | : | 9776-03 | 9779-03 | 9780-02 | 9781-02 |
| DAYS ON TEST | : | 24 | 22 | 24 | 24 |
| DATE OF NECROPSY | : | 18-NOV-03 | 14-NOV-03 | 17-NOV-03 | 17-NOV-03 |
| DEFND./ACTUAL NECR.STATE: | | K0/K0 | K0/K0 | K0/K0 | K0/K0 |
| | | | | | |
| FINAL BODY WEIGHT | G: | 63.5070 | 58.4170 | 68.4750 | 58.5630 |
| | | | | | |
| BRAIN | G: | 1.5400 | 1.4980 | 1.4600 | 1.4010 |
| | % BODY : | 2.425 | 2.564 | 2.132 | 2.392 |
| | | | | | |
| SPLEEN | G: | 0.4270 | 0.2050 | 0.3280 | 0.2990 |
| | % BODY : | 0.67237 | 0.35093 | 0.47901 | 0.51056 |
| | % BRAIN: | 27.727 | 13.685 | 22.466 | 21.342 |
| | | | | | |
| THYMUS | G: | 0.2930 | 0.2590 | 0.2820 | 0.2680 |
| | % BODY : | 0.46137 | 0.44336 | 0.41183 | 0.45763 |
| | % BRAIN: | 19.026 | 17.290 | 19.315 | 19.129 |
| | | | | | |

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 TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS
 F2 PUPS

DOSE GROUP : 4, 1000mg/kg/d.F2P
 SEX : MALE

| | | | | | |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| ANIMAL NUMBER | : | 9782-02 | 9783-02 | 9784-02 | 9785-02 |
| DAYS ON TEST | : | 22 | 24 | 22 | 22 |
| DATE OF NECROPSY | : | 14-NOV-03 | 17-NOV-03 | 14-NOV-03 | 14-NOV-03 |
| DEFND./ACTUAL NECR.STATE: | | K0/K0 | K0/K0 | K0/K0 | K0/K0 |
| | | | | | |
| FINAL BODY WEIGHT | G: | 47.9610 | 64.5040 | 52.9560 | 55.8600 |
| | | | | | |
| BRAIN | G: | 1.3700 | 1.4280 | 1.4530 | 1.4750 |
| | % BODY : | 2.856 | 2.214 | 2.744 | 2.641 |
| | | | | | |
| SPLEEN | G: | 0.2580 | 0.3990 | 0.2460 | 0.2390 |
| | % BODY : | 0.53794 | 0.61857 | 0.46454 | 0.42786 |
| | % BRAIN: | 18.832 | 27.941 | 16.930 | 16.203 |
| | | | | | |
| THYMUS | G: | 0.3440 | 0.2720 | 0.2130 | 0.2790 |
| | % BODY : | 0.71725 | 0.42168 | 0.40222 | 0.49946 |
| | % BRAIN: | 25.109 | 19.048 | 14.659 | 18.915 |
| | | | | | |

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 TOTAL France S.A.

 TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS
 F2 PUPS

DOSE GROUP : 4, 1000mg/kg/d.F2P
 SEX : MALE

| | | 9788-02 | 9789-03 | 9790-02 | 9791-03 |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| ANIMAL NUMBER | : | 9788-02 | 9789-03 | 9790-02 | 9791-03 |
| DAYS ON TEST | : | 22 | 24 | 24 | 22 |
| DATE OF NECROPSY | : | 14-NOV-03 | 17-NOV-03 | 17-NOV-03 | 13-NOV-03 |
| DEFND./ACTUAL NECR.STATE: | | K0/K0 | K0/K0 | K0/K0 | K0/K0 |
| | | | | | |
| FINAL BODY WEIGHT | G: | 60.5290 | 69.9600 | 69.5910 | 59.9250 |
| | | | | | |
| BRAIN | G: | 1.6000 | 1.5900 | 1.5450 | 1.5860 |
| | % BODY : | 2.643 | 2.273 | 2.220 | 2.647 |
| | | | | | |
| SPLEEN | G: | 0.2770 | 0.2960 | 0.2910 | 0.2810 |
| | % BODY : | 0.45763 | 0.42310 | 0.41816 | 0.46892 |
| | % BRAIN: | 17.313 | 18.616 | 18.835 | 17.718 |
| | | | | | |
| THYMUS | G: | 0.2720 | 0.3220 | 0.2570 | 0.2020 |
| | % BODY : | 0.44937 | 0.46026 | 0.36930 | 0.33709 |
| | % BRAIN: | 17.000 | 20.252 | 16.634 | 12.736 |
| | | | | | |

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 TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS
 F2 PUPS

DOSE GROUP : 4, 1000mg/kg/d.F2P
 SEX : MALE

| | | 9792-02 | 9793-03 | 9794-03 | 9795-02 |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| ANIMAL NUMBER | : | 9792-02 | 9793-03 | 9794-03 | 9795-02 |
| DAYS ON TEST | : | 24 | 22 | 22 | 22 |
| DATE OF NECROPSY | : | 17-NOV-03 | 13-NOV-03 | 13-NOV-03 | 14-NOV-03 |
| DEFND./ACTUAL NECR.STATE: | | K0/K0 | K0/K0 | K0/K0 | K0/K0 |
| | | | | | |
| FINAL BODY WEIGHT | G: | 65.6410 | 60.5130 | 50.0470 | 55.8650 |
| | | | | | |
| BRAIN | G: | 1.5610 | 1.3440 | 1.4050 | 1.4260 |
| | % BODY : | 2.378 | 2.221 | 2.807 | 2.553 |
| | | | | | |
| SPLEEN | G: | 0.3150 | 0.2730 | 0.2230 | 0.3010 |
| | % BODY : | 0.47988 | 0.45114 | 0.44558 | 0.53880 |
| | % BRAIN: | 20.179 | 20.313 | 15.872 | 21.108 |
| | | | | | |
| THYMUS | G: | 0.3080 | 0.2660 | 0.2250 | 0.2110 |
| | % BODY : | 0.46922 | 0.43957 | 0.44958 | 0.37770 |
| | % BRAIN: | 19.731 | 19.792 | 16.014 | 14.797 |
| | | | | | |

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TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS
F2 PUPS

DOSE GROUP : 4, 1000mg/kg/d.F2P
SEX : MALE

| | | | | |
|---------------------------|---|-----------|-----------|-----------|
| ANIMAL NUMBER | : | 9796-03 | 9797-03 | 9800-02 |
| DAYS ON TEST | : | 22 | 22 | 24 |
| DATE OF NECROPSY | : | 12-NOV-03 | 13-NOV-03 | 17-NOV-03 |
| DEFND./ACTUAL NECR.STATE: | | K0/K0 | K0/K0 | K0/K0 |

.....
FINAL BODY WEIGHT G: 55.9570 48.7380 62.1740
.....

| | | | | |
|-------|----------|--------|--------|--------|
| BRAIN | G: | 1.2870 | 1.3980 | 1.4670 |
| | % BODY : | 2.300 | 2.868 | 2.360 |

.....
SPLEEN G: 0.2700 0.2500 0.3070
% BODY : 0.48251 0.51295 0.49378
% BRAIN: 20.979 17.883 20.927
.....

| | | | | |
|--------|----------|---------|---------|---------|
| THYMUS | G: | 0.2950 | 0.2300 | 0.2600 |
| | % BODY : | 0.52719 | 0.47191 | 0.41818 |
| | % BRAIN: | 22.922 | 16.452 | 17.723 |

.....

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 F2 PUPS

DOSE GROUP : 4, 1000mg/kg/d.F2P
 SEX : FEMALE

| | | | | | |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| ANIMAL NUMBER | : | 9776-07 | 9779-10 | 9780-10 | 9781-10 |
| DAYS ON TEST | : | 24 | 22 | 24 | 24 |
| DATE OF NECROPSY | : | 18-NOV-03 | 14-NOV-03 | 17-NOV-03 | 17-NOV-03 |
| DEFND./ACTUAL NECR.STATE: | | K0/K0 | K0/K0 | K0/K0 | K0/K0 |
| | | | | | |
| FINAL BODY WEIGHT | G: | 61.7590 | 52.9920 | 66.9350 | 57.3840 |
| | | | | | |
| BRAIN | G: | 1.4690 | 1.4070 | 1.5120 | 1.4310 |
| | % BODY : | 2.379 | 2.655 | 2.259 | 2.494 |
| | | | | | |
| SPLEEN | G: | 0.3060 | 0.2180 | 0.2480 | 0.2840 |
| | % BODY : | 0.49547 | 0.41138 | 0.37051 | 0.49491 |
| | % BRAIN: | 20.830 | 15.494 | 16.402 | 19.846 |
| | | | | | |
| THYMUS | G: | 0.2850 | 0.2330 | 0.3100 | 0.2680 |
| | % BODY : | 0.46147 | 0.43969 | 0.46314 | 0.46703 |
| | % BRAIN: | 19.401 | 16.560 | 20.503 | 18.728 |
| | | | | | |

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 F2 PUPS

DOSE GROUP : 4, 1000mg/kg/d.F2P
 SEX : FEMALE

| | | | | | |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| ANIMAL NUMBER | : | 9782-11 | 9783-09 | 9784-14 | 9785-11 |
| DAYS ON TEST | : | 22 | 24 | 22 | 22 |
| DATE OF NECROPSY | : | 14-NOV-03 | 17-NOV-03 | 14-NOV-03 | 14-NOV-03 |
| DEFND./ACTUAL NECR.STATE: | | K0/K0 | K0/K0 | K0/K0 | K0/K0 |
| | | | | | |
| FINAL BODY WEIGHT | G: | 43.4370 | 62.4810 | 47.4510 | 58.5850 |
| | | | | | |
| BRAIN | G: | 1.2830 | 1.5140 | 1.4470 | 1.4030 |
| | % BODY : | 2.954 | 2.423 | 3.049 | 2.395 |
| | | | | | |
| SPLEEN | G: | 0.2000 | 0.3240 | 0.1680 | 0.2700 |
| | % BODY : | 0.46044 | 0.51856 | 0.35405 | 0.46087 |
| | % BRAIN: | 15.588 | 21.400 | 11.610 | 19.244 |
| | | | | | |
| THYMUS | G: | 0.2050 | 0.3520 | 0.2220 | 0.3400 |
| | % BODY : | 0.47195 | 0.56337 | 0.46785 | 0.58035 |
| | % BRAIN: | 15.978 | 23.250 | 15.342 | 24.234 |
| | | | | | |

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TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS
F2 PUPS

DOSE GROUP : 4, 1000mg/kg/d.F2P
SEX : FEMALE

| | | | | | |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| ANIMAL NUMBER | : | 9788-10 | 9789-10 | 9790-09 | 9791-09 |
| DAYS ON TEST | : | 22 | 24 | 24 | 22 |
| DATE OF NECROPSY | : | 14-NOV-03 | 17-NOV-03 | 17-NOV-03 | 13-NOV-03 |
| DEFND./ACTUAL NECR.STATE: | | K0/K0 | K0/K0 | K0/K0 | K0/K0 |
| | | | | | |
| FINAL BODY WEIGHT | G: | 56.2730 | 71.8850 | 62.3540 | 55.1680 |
| | | | | | |
| BRAIN | G: | 1.4620 | 1.4400 | 1.5000 | 1.5050 |
| | % BODY : | 2.598 | 2.003 | 2.406 | 2.728 |
| | | | | | |
| SPLEEN | G: | 0.2480 | 0.2170 | 0.3270 | 0.2310 |
| | % BODY : | 0.44071 | 0.30187 | 0.52443 | 0.41872 |
| | % BRAIN: | 16.963 | 15.069 | 21.800 | 15.349 |
| | | | | | |
| THYMUS | G: | 0.2400 | 0.3400 | 0.3000 | 0.2370 |
| | % BODY : | 0.42649 | 0.47298 | 0.48112 | 0.42960 |
| | % BRAIN: | 16.416 | 23.611 | 20.000 | 15.748 |
| | | | | | |

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
 TOTAL France S.A.

 TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS
 F2 PUPS

DOSE GROUP : 4, 1000mg/kg/d.F2P
 SEX : FEMALE

| | | | | | |
|---------------------------|----------|-----------|-----------|-----------|-----------|
| ANIMAL NUMBER | : | 9792-10 | 9793-08 | 9794-11 | 9795-07 |
| DAYS ON TEST | : | 24 | 22 | 22 | 22 |
| DATE OF NECROPSY | : | 17-NOV-03 | 13-NOV-03 | 13-NOV-03 | 14-NOV-03 |
| DEFND./ACTUAL NECR.STATE: | | K0/K0 | K0/K0 | K0/K0 | K0/K0 |
| | | | | | |
| FINAL BODY WEIGHT | G: | 56.4390 | 51.0430 | 50.2910 | 51.2140 |
| | | | | | |
| BRAIN | G: | 1.4500 | 1.4010 | 1.4050 | 1.3600 |
| | % BODY : | 2.569 | 2.745 | 2.794 | 2.656 |
| | | | | | |
| SPLEEN | G: | 0.3430 | 0.2490 | 0.2600 | 0.2670 |
| | % BODY : | 0.60774 | 0.48782 | 0.51699 | 0.52134 |
| | % BRAIN: | 23.655 | 17.773 | 18.505 | 19.632 |
| | | | | | |
| THYMUS | G: | 0.2600 | 0.2110 | 0.2250 | 0.2280 |
| | % BODY : | 0.46067 | 0.41338 | 0.44740 | 0.44519 |
| | % BRAIN: | 17.931 | 15.061 | 16.014 | 16.765 |
| | | | | | |

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TABLE OF INDIVIDUAL BODY/ORGAN WEIGHTS
F2 PUPS

DOSE GROUP : 4, 1000mg/kg/d.F2P
SEX : FEMALE

| | | | | |
|---------------------------|---|-----------|-----------|-----------|
| ANIMAL NUMBER | : | 9796-11 | 9797-08 | 9800-08 |
| DAYS ON TEST | : | 22 | 22 | 24 |
| DATE OF NECROPSY | : | 12-NOV-03 | 13-NOV-03 | 17-NOV-03 |
| DEFND./ACTUAL NECR.STATE: | | K0/K0 | K0/K0 | K0/K0 |

.....
FINAL BODY WEIGHT G: 54.0540 50.8810 57.8210
.....

| | | | | |
|-------|----------|--------|--------|--------|
| BRAIN | G: | 1.3100 | 1.4180 | 1.4080 |
| | % BODY : | 2.424 | 2.787 | 2.435 |

| | | | | |
|--------|----------|---------|---------|---------|
| SPLEEN | G: | 0.2810 | 0.2580 | 0.2940 |
| | % BODY : | 0.51985 | 0.50707 | 0.50847 |
| | % BRAIN: | 21.450 | 18.195 | 20.881 |

| | | | | |
|--------|----------|---------|---------|---------|
| THYMUS | G: | 0.3020 | 0.2800 | 0.2600 |
| | % BODY : | 0.55870 | 0.55030 | 0.44966 |
| | % BRAIN: | 23.053 | 19.746 | 18.466 |

.....

SPONSOR

TOTAL France S.A.
Tour Galilée
51 Esplanade du Général de Gaulle
La Défense 10
92907 Paris-la-Défense CEDEX
France

On behalf of:

CEPSA
ENI S.p.A.
Fortum Oil and Gas Oy
Lyondell Chemical Europe Inc.
Oxeno Olefinchemie GmbH
Repsol Petróleo, S.A.
TOTAL France S.A.

TEST ITEM

ETHYL TERTIARY BUTYL ETHER (ETBE)
CAS No. 637-92-3

STUDY TITLE

TWO-GENERATION STUDY
(REPRODUCTION AND FERTILITY EFFECTS)
BY ORAL ROUTE (GAVAGE) IN RATS

STUDY DIRECTOR

Wassila Gaoua

EXPERIMENTAL COMPLETION DATE

12 December 2003

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TEST FACILITY

CIT
BP 563 - 27005 Evreux - France

LABORATORY STUDY NUMBER

24859 RSR

Volume 5

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APPENDICES (continued)

67. F1 generation - individual macroscopic and microscopic examinations

EXPLANATION OF CODES AND SYMBOLS

CODES AND SYMBOLS USED AT ANIMAL LEVEL:

M = Male animal
F = Female animal
K0 = Terminal sacrifice group
+ = Intercurrent death/sacrificed moribund
+1 = Found dead
+2 = Sacrificed moribund

CODES AND SYMBOLS USED AT ORGAN LEVEL:

G = Gross observation checked off histologically
! = Gross observat.not checked off histologically
* = Comment in text of individual animal data
0 = Tissue not present for histologic examination
' = Histologic examination not required
+ = Organ examined, findings present
- = Organ examined, no pathologic findings noted (AOFT only)
(= Only one of paired organs examined/present

CODES AND SYMBOLS USED AT FINDING LEVEL:

GRADE 1 = Minimal / very few / very small
GRADE 2 = Slight / few / small
GRADE 3 = Moderate / moderate number / moderate size
GRADE 4 = Marked / many / large
GRADE 5 = Massive / extensive number / extensive size
P = Finding present, severity not scored
B0 = Benign neoplasm
N0 = Malignant neoplasm
(= Finding unilateral in paired organs
* = Comment in text of individual animal data

EXPLANATION OF TABLE TEXT(S) USED AT FINDING LEVEL:

ADRENAL GLANDS

- Acces. adrenal cort.
 = Accessory adrenal cortex
- Altered Cell Foci
 = Altered cell foci
- Cort.Cel.Hypertrophy

EXPLANATION OF CODES AND SYMBOLS

EXPLANATION OF TABLE TEXT(S) USED AT FINDING LEVEL:

- Cyst(s)
 - = Cortical cell hypertrophy
 - Cyst(s)
 - = Cyst(s)
 - Cystic Degeneration
 - = Cystic degeneration
 - Inters.Mono.Cel.Agg.
 - = Interstitial mononuclear cell aggregation
 - Lipomatosis
 - = Lipomatosis
 - Sinusoidal Ectasia
 - = Sinusoidal ectasia sometimes with blood extravasation
 - Vacuol.Cortical cell
 - = Vacuolated cortical cell
- PITUITARY GLAND
- Cyst(s)
 - = Cyst(s)
 - Development. Cyst(S)
 - = Developmental cyst(s)
 - Vacuolated Cells
 - = Vacuolated cells
- OVARIES
- Diestrus
 - = Diestrus
 - Estrus
 - = Estrus
 - Metestrus
 - = Metestrus
 - Pregn.Corpora Lutea
 - = Pregnancy corpora lutea
 - Proestrus
 - = Proestrus
- UTERUS
- Diestrus
 - = Diestrus
 - Dilated Lumen
 - = Dilated lumen
 - Estrus
 - = Estrus
 - Infold.end.epithel.

EXPLANATION OF CODES AND SYMBOLS

EXPLANATION OF TABLE TEXT(S) USED AT FINDING LEVEL:

- = Infolding endometrial epithelium
- Metestrus
 - = Metestrus
- Mineralization
 - = Mineralization
- Morphology of Pregn.
 - = Morphology of pregnancy
- Proestrus
 - = Proestrus
- Yell.pigm.lad.macro.
 - = Yellowish pigment laden macrophages

VAGINA

- Diestrus
 - = Diestrus
- Epithel.Cel.Hyperpl.
 - = Epithelial cell hyperplasia
- Estrus
 - = Estrus
- Metestrus
 - = Metestrus
- Mucific.Vagin.Epith.
 - = Mucification vaginal epithelium
- Proestrus
 - = Proestrus

PROSTATE

- Acute Prostatitis
 - = Acute Prostatitis
- Atroph.Tub.Alv.Units
 - = Atrophy of tubulo-alveolar units
- Epithel.Cell Atrophy
 - = Epithelial cell atrophy
- Granulocyte Infiltr.
 - = Granulocyte infiltration
- Hypersecretion
 - = Hypersecretion
- Inters.Mono.Cel.Agg.
 - = Interstitial mononuclear cell aggregation
- Subacute Prostatitis
 - = Subacute prostatitis

EXPLANATION OF CODES AND SYMBOLS

EXPLANATION OF TABLE TEXT(S) USED AT FINDING LEVEL:

SEMINAL VESICLES+ COAGULATING GLANDS

- Inters.Mono.Cel.Agg.
 - = Interstitial mononuclear cell aggregation

TESTIS, RIGHT

- Deg./Necr.Cel.Sloug.
 - = Degenerated/necrotic cells sloughed in lumen
- Degener.germ.epith.
 - = Degeneration of germinal epithelium
- Diff.Stag.Cycl.Dist.
 - = Different stages of cycle disturbed
- Diff.Stag.Cycl.Pres.
 - = Different stages of spermatogenic cycle present
- Multinucl.Giant Cel.
 - = Multinucleated Giant Cells
- Reduc.Round spermat.
 - = Reduced round spermatids
- Reduc.Tailed.Sperma.
 - = Reduced number of tailed spermatids
- Retained Spermatids
 - = Retained spermatids (stage 19 within tubules of stage>IX)
- Round Sperm.Norm.Nu.
 - = Round spermatids (steps 1-9) present/normal number
- Sem.tub.lin.Sert.c.
 - = Seminiferous tubules lined by Sertoli cells only
- Spermatic Granuloma
 - = Spermatic granuloma
- Spermatoc.Norm.Numb.
 - = Spermatocytes present/normal number
- Spermatocy.Reduced
 - = Spermatocytes reduced in number
- Spermatog.Normal Nu.
 - = Spermatogonia present/normal number
- Spermatogonia Reduc.
 - = Spermatogonia Reduced
- Tail.Sperm.Norm.Num.
 - = Tailed spermatids (steps 10-19) present/normal number
- Vacuol.semin.tubules
 - = Vacuolated seminiferous tubules
- Vacuol.sertoli cells

EXPLANATION OF CODES AND SYMBOLS

EXPLANATION OF TABLE TEXT(S) USED AT FINDING LEVEL:

- = Vacuolated sertoli cells
- EPIDIDYMIS (RIGHT)
- Aspermia
 - = Aspermia
- Exfol.Sperm.Sloughed
 - = Exfoliated spermatids sloughed in epididymal ducts
- Inters.Mono.Cel.Agg.
 - = Interstitial mononuclear cell aggregation
- Oligospermia
 - = Oligospermia
- LIVER
- Alt.cel.foci acid.
 - = Altered cell foci acidophilic
- Alt.cel.foci clear
 - = Altered cell foci clear
- Hepatocel.Hypertrop.
 - = Hepatocellular hypertrophy
- Mononuclear Cel.Agg.
 - = Mononuclear cell aggregation
- KIDNEYS
- Aci.Glob.Cor.Tub.Ep.
 - = Acidophilic globules in cortical tubular epithelium
- Deg./Necr.C.Sloughed
 - = Degenerated/necrotic cells sloughed in tubular lumens
- Dilated Pelvis
 - = Dilated pelvis
- Inters.Mono.Cel.Agg.
 - = Interstitial mononuclear cell aggregation
- Nephroblastoma
 - = Nephroblastoma
- Peritubular Fibrosis
 - = Peritubular fibrosis
- Tubular Basophilia
 - = Tubular basophilia
- Tubular Dilatation
 - = Tubular dilatation
- SPLEEN
- Extramed.hematopoi.
 - = Extramedullary hematopoiesis

EXPLANATION OF CODES AND SYMBOLS

EXPLANATION OF TABLE TEXT(S) USED AT FINDING LEVEL:

- Lymphoid Cel.Hyperp.
= Lymphoid cell hyperplasia

THYMUS

- Capillary hemorrhage
= Capillary hemorrhage

PALPABLE MASSES

- Mammary Fibroadenoma
= Mammary Fibroadenoma

ADIPOSE TISSUE

- Fat Necrosis
= Fat necrosis

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

ANIMAL NUMBER : B2 B2 B2 B2 B2 B2 B2 B2 B2 B2
 9301 9302 9303 9304 9305 9306 9307 9308 9309 9310
 MK0 MK0 MK0 MK0+ MK0 MK0 MK0 MK0 MK0 MK0

SPLEEN ' ' ' ' ! ' ' ' ' ' '
.....

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
 TOTAL France S.A.

 TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

 ANIMAL NUMBER : B2 B2 B2 B2 B2
 9321 9322 9323 9324 9325
 MK0 MK0 MK0 MK0 MK0

 ADRENAL GLANDS - - - - +
 - Acces. adrenal cort. (P.
 - Sinusoidal Ectasia 2.

.....
 PITUITARY GLAND - + + - -
 - Vacuolated Cells . 1. 2. . .

.....
 PROSTATE + + + + +
 - Epithel.Cell Atrophy 1. . 1. 1. 3.
 - Inters.Mono.Cel.Agg. 1.
 - Subacute Prostatitis . 2. . . .

.....
 SEMINAL VESICLES - - - - +
 - Inters.Mono.Cel.Agg. (1*

.....
 TESTIS, RIGHT + + + + +
 - Tail.Sperm.Norm.Num. P. P. P. P. P.
 - Round Sperm.Norm.Nu. P. P. P. P. P.
 - Spermatoc.Norm.Numb. P. P. P. P. P.
 - Spermatog.Normal Nu. P. P. P. P. P.
 - Diff.Stag.Cycl.Pres. P. P. P. P. P.
 - Deg./Necr.Cel.Sloug. 1. . . 1. 1.
 - Sem.tub.lin.Sert.c. 1. . . 1. 1.
 - Vacuol.semin.tubules 1. 1. 1. . 1.

.....
 EPIDIDYMIS, RIGHT - - - - -

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
 TOTAL France S.A.

 TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

 ANIMAL NUMBER : B2 B2 B2 B2 B2
 9721 9722 9723 9724 9725
 FK0 FK0 FK0 FK0 FK0

 ADRENAL GLANDS + + + + +
 - Sinusoidal Ectasia (2. 1. 1. 2. 1.

 PITUITARY GLAND - - - - -

 OVARIES + + + + +
 - Proestrus . P. . . .
 - Estrus P.
 - Metestrus P. . P. . .
 - Diestrus . . . P. .

 OVIDUCTS - - (- - -

 UTERUS + +G + + +
 - Proestrus . P. . . .
 - Estrus P.
 - Metestrus P. . P. . .
 - Diestrus . . . P. .
 - Yell.pigm.lad.macro. 1* . . . 2.
 - Dilated Lumen . 3. . . .
 - Mineralization 1.

 VAGINA + + + + +
 - Proestrus . P. . . .
 - Estrus P.
 - Metestrus P. . P. . .
 - Diestrus . . . P. .

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
 TOTAL France S.A.

 TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

| ANIMAL NUMBER : | B2 | B2 | B2 | B2 | B2 | B2 | B2 | B2 | B2 | B2 |
|-------------------------|------|------|------|------|------|------|------|------|------|------|
| | 9336 | 9337 | 9338 | 9339 | 9340 | 9341 | 9342 | 9343 | 9344 | 9345 |
| | MK0 | MK0 | MK0 | MK0 | MK0 | MK0 | MK0 | MK0 | MK0 | MK0 |
| ADRENAL GLANDS | ' | ' | ' | ' | ' | -G | ' | ' | ' | ' |
| PROSTATE | ' | ' | ' | ' | ' | + | ' | ' | ' | ' |
| - Epithel.Cell Atrophy | | | | | | 4. | | | | |
| SEMINAL VESICLES | ' | ' | ' | ' | ' | - | ' | ' | ' | ' |
| TESTIS, RIGHT | + | + | + | + | + | + | + | + | + | + |
| - Tail.Sperm.Norm.Num. | P. | P. | P. | P. | . | P. | P. | P. | P. | P. |
| - Reduc.Tailed.Sperma. | . | . | . | . | 5. | . | . | . | . | . |
| - Round Sperm.Norm.Nu. | P. | P. | P. | P. | . | P. | P. | P. | P. | P. |
| - Reduc.Round spermat. | . | . | . | . | 5. | . | . | . | . | . |
| - Spermatoch.Norm.Numb. | P. | P. | P. | P. | . | P. | P. | P. | P. | P. |
| - Spermatoch.Reduced | . | . | . | . | 5. | . | . | . | . | . |
| - Spermatoch.Normal Nu. | P. | P. | P. | P. | . | P. | P. | P. | P. | P. |
| - Spermatoch.Reduc. | . | . | . | . | 5. | . | . | . | . | . |
| - Diff.Stag.Cycl.Pres. | P. | P. | P. | P. | . | P. | P. | P. | P. | P. |
| - Diff.Stag.Cycl.Dist. | . | . | . | . | 5. | . | . | . | . | . |
| - Deg./Necr.Cel.Sloug. | . | . | . | 1. | . | . | . | . | . | . |
| - Sem.tub.lin.Sert.c. | . | 1* | . | 1* | 5. | . | . | . | . | . |
| - Vacuol.semin.tubules | . | 1. | . | 1. | . | . | . | 1. | . | . |
| - Vacuol.sertoli cells | . | . | . | . | 3. | . | . | . | . | . |
| - Multinucl.Giant Cel. | . | . | . | . | . | . | . | . | . | 1. |
| EPIDIDYMIS, RIGHT | ' | ' | ' | ' | ' | - | ' | ' | ' | ' |
| TESTIS, LEFT | ' | ' | ' | ' | ' | 0 | ' | ' | ' | ' |
| TESTES | ' | ' | ' | ' | G | G | ' | ' | ' | ' |
| EPIDIDYMIDES | ' | ' | ' | ' | 'G | ' | ' | ' | ' | ' |

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

ANIMAL NUMBER : B2 B2 B2 B2 B2 B2 B2 B2 B2 B2
 9726 9727 9728 9729 9730 9731 9732 9733 9734 9735
 FK0 FK0 FK0 FK0 FK0 FK0 FK0 FK0 FK0 FK0

UTERUS ' ' ! ' ' ' ' ' ' ' '
.....

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
 TOTAL France S.A.

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS
 DOSE GROUP : 2, 250mg/kg/d.F1

| ANIMAL NUMBER : | B2 | B2 | B2 | B2 | B2 |
|-----------------|------|------|------|------|------|
| | 9746 | 9747 | 9748 | 9749 | 9750 |
| | FK0 | FK0 | FK0 | FK0 | FK0 |
| OVARIES | + | ' | ' | ' | ' |
| - Estrus | P. | | | | |
| | | | | | |
| OVIDUCTS | - | ' | ' | ' | ' |
| | | | | | |
| UTERUS | -* | '! | ' | ' | ' |
| | | | | | |
| VAGINA | + | ' | ' | ' | ' |
| - Estrus | P. | | | | |
| | | | | | |

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

| ANIMAL NUMBER : | B2 | B2 | B2 | B2 | B2 | B2 | B2 | B2 | B2 | B2 |
|------------------------|------|------|------|------|------|------|------|------|------|------|
| | 9361 | 9362 | 9363 | 9364 | 9365 | 9366 | 9367 | 9368 | 9369 | 9370 |
| | MK0 | MK0 | MK0 | MK0 | MK0 | MK0 | MK0 | MK0 | MK0 | MK0 |
| PROSTATE | ' | ' | ' | ' | ' | ' | ' | + | ' | ' |
| - Inters.Mono.Cel.Agg. | | | | | | | | 1. | | |
| SEMINAL VESICLES | ' | ' | ' | ' | ' | ' | ' | - | ' | ' |
| TESTIS, RIGHT | + | + | + | + | + | + | + | + | + | + |
| - Tail.Sperm.Norm.Num. | P. | P. | P. | P. | P. | P. | P. | P. | P. | P. |
| - Round Sperm.Norm.Nu. | P. | P. | P. | P. | P. | P. | P. | P. | P. | P. |
| - Spermatoc.Norm.Numb. | P. | P. | P. | P. | P. | P. | P. | P. | P. | P. |
| - Spermatog.Normal Nu. | P. | P. | P. | P. | P. | P. | P. | P. | P. | P. |
| - Diff.Stag.Cycl.Pres. | P. | P. | P. | P. | P. | P. | P. | P. | P. | P. |
| - Deg./Necr.Cel.Sloug. | . | 1. | . | . | . | 2. | . | . | . | . |
| - Sem.tub.lin.Sert.c. | . | 1. | . | . | . | . | 1* | 1. | . | . |
| - Vacuol.semin.tubules | . | 1. | . | . | . | . | . | . | . | . |
| - Vacuol.sertoli cells | . | 1. | . | . | . | . | . | . | . | . |
| EPIDIDYMIS, RIGHT | ' | ' | ' | ' | ' | ' | ' | - | ' | ' |
| KIDNEYS | ' | ' | '! | ' | ' | ' | ' | ' | '! | '! |

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
 TOTAL France S.A.

 TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

 ANIMAL NUMBER : B2 B2 B2 B2 B2
 9371 9372 9373 9374 9375
 MK0 MK0 MK0 MK0 MK0+

 TESTIS, RIGHT + + + + '
 - Tail.Sperm.Norm.Num. P. P. P. P.
 - Round Sperm.Norm.Nu. P. P. P. P.
 - Spermatoc.Norm.Numb. P. P. P. P.
 - Spermatog.Normal Nu. P. P. P. P.
 - Diff.Stag.Cycl.Pres. P. P. P. P.
 - Deg./Necr.Cel.Sloug. . . 2. 1*
 - Sem.tub.lin.Sert.c. . . 1* 1*
 - Vacuol.semin.tubules 1. . . 1.

.....
 LUNGS ' ' ' ' ' !

.....
 ADIPOSE TISSUE ' ' ! ' ' '

.....

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

ANIMAL NUMBER : B2 B2 B2 B2 B2 B2 B2 B2 B2 B2
 9751 9752 9753 9754 9755 9756 9757 9758 9759 9760
 FK0 FK0 FK0 FK0 FK0 FK0 FK0 FK0 FK0 FK0

UTERUS ' ' ' ' ' ' ' ' ' '
.....

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

ANIMAL NUMBER : B2 B2 B2 B2 B2
 9771 9772 9773 9774 9775
 FK0 FK0 FK0 FK0 FK0

OVARIES ' ' + ' '
- Proestrus P.

.....
OVIDUCTS ' ' - ' '

.....
UTERUS ' ! ' -G ' '

.....
VAGINA ' ' + ' '
- Proestrus P.

.....

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

| ANIMAL NUMBER : | B2 | B2 | B2 | B2 | B2 | B2 | B2 | B2 | B2 | B2 |
|------------------------|------|------|------|------|------|------|------|------|------|------|
| | 9376 | 9377 | 9378 | 9379 | 9380 | 9381 | 9382 | 9383 | 9384 | 9385 |
| | MK0 | MK0 | MK0 | MK0 | MK0 | MK0 | MK0 | MK0 | MK0 | MK0 |
| ADRENAL GLANDS | + | + | + | + | + | - | + | + | + | + |
| - Acces. adrenal cort. | . | (P. | . | (P. | . | . | . | . | . | . |
| - Inters.Mono.Cel.Agg. | . | . | . | . | 1. | . | 1. | . | . | . |
| - Sinusoidal Ectasia | . | (1. | . | (1. | . | . | . | (1. | 1. | (1. |
| - Cyst(s) | . | . | . | . | . | . | . | . | . | (P. |
| - Vacuol.Cortical cell | 2. | . | . | 2. | . | . | . | . | . | . |
| - Lipomatosis | . | . | (1. | . | . | . | . | . | . | . |
| PITUITARY GLAND | - | - | - | + | + | + | - | - | - | - |
| - Vacuolated Cells | . | . | . | 1. | 1. | 1. | . | . | . | . |
| PROSTATE | + | + | - | + | - | + | - | + | + | + |
| - Hypersecretion | . | . | . | 2. | . | . | . | . | . | . |
| - Epithel.Cell Atrophy | . | 1. | . | 2. | . | 2. | . | . | 2. | 1. |
| - Inters.Mono.Cel.Agg. | 1. | . | . | . | . | . | . | 1. | . | . |
| - Acute Prostatitis | . | 1. | . | . | . | . | . | . | . | . |
| - Subacute Prostatitis | . | 2. | . | . | . | 3. | . | . | . | . |
| SEMINAL VESICLES | - | - | - | - | - | - | - | - | - | - |
| TESTIS, RIGHT | + | + | + | + | + | + | + | + | + | + |
| - Tail.Sperm.Norm.Num. | P. | P. | P. | P. | P. | . | P. | P. | P. | P. |
| - Reduc.Tailed.Sperma. | . | . | . | . | . | 5. | . | . | . | . |
| - Round Sperm.Norm.Nu. | P. | P. | P. | P. | P. | . | P. | P. | P. | P. |
| - Reduc.Round spermat. | . | . | . | . | . | 5. | . | . | . | . |
| - Spermatoc.Norm.Numb. | P. | P. | P. | P. | P. | . | P. | P. | P. | P. |
| - Spermatocy.Reduced | . | . | . | . | . | 5. | . | . | . | . |
| - Spermatog.Normal Nu. | P. | P. | P. | P. | P. | . | P. | P. | P. | P. |
| - Spermatogonia Reduc. | . | . | . | . | . | 5. | . | . | . | . |
| - Diff.Stag.Cycl.Pres. | P. | P. | P. | P. | P. | . | P. | P. | P. | P. |
| - Diff.Stag.Cycl.Dist. | . | . | . | . | . | 5. | . | . | . | . |
| - Deg./Necr.Cel.Sloug. | . | . | . | 1. | . | . | . | . | 2. | . |
| - Sem.tub.lin.Sert.c. | . | . | . | 1. | . | 5. | 1. | . | 2. | . |
| - Vacuol.semin.tubules | . | . | . | 1. | . | . | 1. | . | . | . |
| - Vacuol.sertoli cells | . | . | . | . | . | . | . | . | 1. | . |
| - Degener.germ.epith. | . | . | . | . | 1. | . | . | . | . | . |
| EPIDIDYMIS, RIGHT | - | - | - | - | - | + | - | - | - | - |
| - Aspermia | . | . | . | . | . | 5. | . | . | . | . |

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

ANIMAL NUMBER : B2 B2 B2 B2 B2
 9396 9397 9398 9399 9400
 MK0 MK0 MK0 MK0 MK0

ADRENAL GLANDS + + + - +
- Inters.Mono.Cel.Agg. 1.
- Sinusoidal Ectasia (1. . 2. . (1.
- Vacuol.Cortical cell . 2. . . 2.
- Altered Cell Foci (1.
- Cystic Degeneration (1.

.....
PITUITARY GLAND + + - + -
- Vacuolated Cells 1. 1. . 2. .

.....
PROSTATE + + + + +
- Epithel.Cell Atrophy . . . 2. 3.
- Inters.Mono.Cel.Agg. . . 1. 1. 1.
- Granulocyte Infiltr. . . . 1. .
- Subacute Prostatitis 3. 1. . . .

.....
SEMINAL VESICLES - - - - -

.....
TESTIS, RIGHT + + + + +
- Tail.Sperm.Norm.Num. P. P. P. P. P.
- Round Sperm.Norm.Nu. P. P. P. P. P.
- Spermatoc.Norm.Numb. P. P. P. P. P.
- Spermatog.Normal Nu. P. P. P. P. P.
- Diff.Stag.Cycl.Pres. P. P. P. P. P.
- Deg./Necr.Cel.Sloug. . . 2. . 2.
- Sem.tub.lin.Sert.c. . . . 1. .

.....
EPIDIDYMIS, RIGHT - - - - +
- Inters.Mono.Cel.Agg. 2.

.....
TESTES ' ' G ' '

.....
EPIDIDYIMIDES ' ' G ' '

.....
LIVER ' ' ' +G '
- Alt.cel.foci acid. . . . 1. .
- Alt.cel.foci clear . . . 1. .
- Mononuclear Cel.Agg. . . . 2* .
- Hepatocel.Hypertrop. . . . 3* .

.....

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
 TOTAL France S.A.

 TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

 ANIMAL NUMBER : B2 B2 B2 B2 B2
 9396 9397 9398 9399 9400
 MK0 MK0 MK0 MK0 MK0

 KIDNEYS ' ' +G +G '
 - Dilated Pelvis (2. .
 - Tubular Basophilia . 1.
 - Peritubular Fibrosis . 1.
 - Aci.Glob.Cor.Tub.Ep. 2. 3.
 - Inters.Mono.Cel.Agg. . (1.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

| ANIMAL NUMBER : | B2 | B2 | B2 | B2 | B2 | B2 | B2 | B2 | B2 | B2 |
|------------------------|------|------|------|------|------|------|------|------|------|------|
| | 9786 | 9787 | 9788 | 9789 | 9790 | 9791 | 9792 | 9793 | 9794 | 9795 |
| | FK0 | FK0 | FK0 | FK0 | FK0 | FK0 | FK0 | FK0 | FK0 | FK0 |
| GENERAL OBSERVATION | ' | ' | ' | '! | ' | ' | ' | ' | ' | ' |
| ADRENAL GLANDS | + | + | + | + | + | + | + | + | + | + |
| - Cort.Cel.Hypertrophy | . | . | . | . | . | . | (2. | . | . | . |
| - Acces. adrenal cort. | . | . | . | . | . | . | . | . | (P. | . |
| - Inters.Mono.Cel.Agg. | . | 1. | . | . | . | . | . | (1. | . | . |
| - Sinusoidal Ectasia | 1. | 1. | 1. | (2. | (1. | (1. | 2. | (2. | 1. | 1. |
| PITUITARY GLAND | - | - | - | - | - | - | - | - | - | - |
| OVARIES | + | + | + | - | - | + | + | + | + | + |
| - Estrus | P. | . | . | . | . | P. | . | . | . | . |
| - Diestrus | . | . | P. | . | . | . | P. | P. | P. | P. |
| - Pregn.Corpora Lutea | . | P. | . | . | . | . | . | . | . | . |
| OVIDUCTS | - | - | - | - | (- | - | (- | (- | - | - |
| UTERUS | -* | + | + | + | + | + | + | + | + | + |
| - Infold.end.epithel. | . | . | . | 3. | . | . | . | . | . | . |
| - Estrus | . | . | . | . | . | P. | . | . | . | . |
| - Diestrus | . | . | P. | . | . | . | P. | P. | P. | P. |
| - Yell.pigm.lad.macro. | . | . | 2* | . | 2. | . | 3* | 2. | . | 2. |
| - Morphology of Pregn. | . | P. | . | . | . | . | . | . | . | . |
| VAGINA | + | + | + | + | + | + | + | + | + | + |
| - Estrus | P. | . | . | . | . | P. | . | . | . | . |
| - Diestrus | . | . | P. | . | . | . | P. | P. | P. | P. |
| - Mucific.Vagin.Epith. | . | 3. | . | 2. | 2. | . | . | . | . | . |

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
 TOTAL France S.A.

 TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

 ANIMAL NUMBER : B2 B2 B2 B2 B2
 9796 9797 9798 9799 9800
 FK0 FK0 FK0 FK0+ FK0

 ADRENAL GLANDS + + + - +
 - Sinusoidal Ectasia (1. 1. 1. . 1.

.....
 PITUITARY GLAND - - - - -

.....
 OVARIES + + + + +
 - Proestrus P.
 - Metestrus . P. . . .
 - Diestrus P. . . P. .
 - Pregn.Corpora Lutea . . P. . .

.....
 OVIDUCTS (- - - (- (-

.....
 UTERUS + + + + +
 - Proestrus P.
 - Metestrus . P. . . .
 - Diestrus P. . . P. .
 - Yell.pigm.lad.macro. 3. 2* . 2* .
 - Morphology of Pregn. . . P. . .

.....
 VAGINA + + + + +
 - Proestrus P.
 - Metestrus . P. . . .
 - Diestrus P. . . P. .
 - Mucific.Vagin.Epith. . . 4. . .

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

ANIMAL HEADING DATA

DOSE GROUP : 1, 0mg/kg/d.F1

| ANIMAL NUMBER | SEX M/F | DEFINED AND FINAL STATE OF NECROPSY | FINAL NECROPSY | TEST DAYS | FIRST AND LAST DAY UNDER TEST | DATE OF NECROPSY |
|------------------|------------|--|-------------------|--------------|----------------------------------|---------------------|
| B29301 | M | K0 | K0 | 125 | 23-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29302 | M | K0 | K0 | 125 | 23-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29303 | M | K0 | K0 | 125 | 23-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29304 | M | K0 | +2 | 37 | 23-JUL-03 28-AUG-03 | 28-AUG-03 |
| B29305 | M | K0 | K0 | 124 | 24-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29306 | M | K0 | K0 | 124 | 24-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29307 | M | K0 | K0 | 124 | 24-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29308 | M | K0 | K0 | 124 | 24-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29309 | M | K0 | K0 | 123 | 25-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29310 | M | K0 | K0 | 123 | 25-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29311 | M | K0 | K0 | 124 | 25-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29312 | M | K0 | K0 | 124 | 25-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29313 | M | K0 | K0 | 124 | 25-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29314 | M | K0 | K0 | 124 | 25-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29315 | M | K0 | K0 | 124 | 25-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29316 | M | K0 | K0 | 125 | 25-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29317 | M | K0 | K0 | 124 | 26-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29318 | M | K0 | K0 | 124 | 26-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29319 | M | K0 | K0 | 124 | 26-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29320 | M | K0 | K0 | 124 | 26-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29321 | M | K0 | K0 | 124 | 26-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29322 | M | K0 | K0 | 123 | 27-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29323 | M | K0 | K0 | 123 | 27-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29324 | M | K0 | K0 | 123 | 27-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29325 | M | K0 | K0 | 123 | 27-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29701 | F | K0 | K0 | 118 | 23-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29702 | F | K0 | K0 | 118 | 23-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29703 | F | K0 | K0 | 104 | 23-JUL-03 03-NOV-03 | 03-NOV-03 |
| B29704 | F | K0 | K0 | 113 | 23-JUL-03 12-NOV-03 | 12-NOV-03 |
| B29705 | F | K0 | K0 | 117 | 24-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29706 | F | K0 | K0 | 117 | 24-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29707 | F | K0 | K0 | 96 | 24-JUL-03 27-OCT-03 | 27-OCT-03 |
| B29708 | F | K0 | K0 | 114 | 24-JUL-03 14-NOV-03 | 14-NOV-03 |
| B29709 | F | K0 | K0 | 112 | 25-JUL-03 13-NOV-03 | 13-NOV-03 |
| B29710 | F | K0 | K0 | 112 | 25-JUL-03 13-NOV-03 | 13-NOV-03 |
| B29711 | F | K0 | K0 | 112 | 25-JUL-03 13-NOV-03 | 13-NOV-03 |
| B29712 | F | K0 | K0 | 95 | 25-JUL-03 27-OCT-03 | 27-OCT-03 |
| B29713 | F | K0 | K0 | 116 | 25-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29714 | F | K0 | K0 | 120 | 25-JUL-03 21-NOV-03 | 21-NOV-03 |
| B29715 | F | K0 | K0 | 117 | 25-JUL-03 18-NOV-03 | 18-NOV-03 |

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

ANIMAL HEADING DATA

DOSE GROUP : 1, 0mg/kg/d.F1

| ANIMAL NUMBER | SEX M/F | DEFINED AND FINAL STATE OF NECROPSY | TEST DAYS | FIRST AND LAST DAY UNDER TEST | DATE OF NECROPSY | |
|------------------|------------|--|--------------|----------------------------------|---------------------|-----------|
| B29716 | F | K0 | K0 | 116 | 25-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29717 | F | K0 | K0 | 116 | 26-JUL-03 18-NOV-03 | 18-NOV-03 |
| B29718 | F | K0 | K0 | 110 | 26-JUL-03 12-NOV-03 | 12-NOV-03 |
| B29719 | F | K0 | K0 | 112 | 26-JUL-03 14-NOV-03 | 14-NOV-03 |
| B29720 | F | K0 | K0 | 89 | 26-JUL-03 22-OCT-03 | 22-OCT-03 |
| B29721 | F | K0 | K0 | 112 | 26-JUL-03 14-NOV-03 | 14-NOV-03 |
| B29722 | F | K0 | K0 | 111 | 27-JUL-03 14-NOV-03 | 14-NOV-03 |
| B29723 | F | K0 | K0 | 111 | 27-JUL-03 14-NOV-03 | 14-NOV-03 |
| B29724 | F | K0 | K0 | 114 | 27-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29725 | F | K0 | K0 | 114 | 27-JUL-03 17-NOV-03 | 17-NOV-03 |

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CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29301 SEX : MALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Degenerated/necrotic cells sloughed in lumen, grade 1
- ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29302 SEX : MALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

TESTES:

01: REDUCED IN SIZE, SOFT.

EPIDIDYMIDES:

01: REDUCED IN SIZE.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

Organ examined, no pathologic findings noted

PITUITARY GLAND:

Organ examined, no pathologic findings noted

PROSTATE:

-Subacute prostatitis, grade 2

SEMINAL VESICLES+ COAGULATING GLANDS:

Organ examined, no pathologic findings noted

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

EPIDIDYMIS (RIGHT):

Organ examined, no pathologic findings noted

TESTES:

Organ not examined

left not examined; no relevant finding on right testis

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

CONT./FF. ANIMAL NO. : B29302
.....

EPIDIDYMIDES:

Organ not examined

left not examined; no relevant finding seen on right epididymis

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29303 SEX : MALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

TESTES:

01: LEFT, REDUCED IN SIZE.

EPIDIDYMIDES:

01: LEFT, REDUCED IN SIZE.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Interstitial mononuclear cell aggregation, unilateral, grade 1

PITUITARY GLAND:

Organ examined, no pathologic findings noted

PROSTATE:

-Interstitial mononuclear cell aggregation, grade 1

SEMINAL VESICLES+ COAGULATING GLANDS:

Organ examined, no pathologic findings noted

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Seminiferous tubules lined by Sertoli cells only, grade 1

EPIDIDYMIS (RIGHT):

Organ examined, no pathologic findings noted

EPIDIDYMIS (LEFT):

Tissue not present for histologic examination

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

CONT./FF. ANIMAL NO. : B29303
.....

TESTIS, LEFT:

Tissue not present for histologic examination

TESTES:

Organ not examined

Tissue with necropsy observation no.01 not submitted for
microscopic examination.

EPIDIDYMIDES:

Organ not examined

Tissue with necropsy observation no.01 not submitted for
microscopic examination.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29304 SEX : MALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 28.08.03
DAYS ON TEST : 37
DATE OF NECROPSY : 28.08.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : SACRIFICED MORIBUND
.....

* NECROPSY FINDINGS

KIDNEYS:

01: PALENESS.

SPLEEN:

01: REDUCED IN SIZE.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29305 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

- Sinusoidal ectasia sometimes with blood extravasation,
unilateral, grade 1
- Cyst(s), unilateral

PITUITARY GLAND:

- Vacuolated cells, grade 1

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
- Round spermatids (steps 1-9) present/normal number
- Spermatocytes present/normal number
- Spermatogonia present/normal number
- Different stages of spermatogenic cycle present
- Degenerated/necrotic cells sloughed in lumen, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29306 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number
-Round spermatids (steps 1-9) present/normal number
-Spermatocytes present/normal number
-Spermatogonia present/normal number
-Different stages of spermatogenic cycle present

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29307 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
- Round spermatids (steps 1-9) present/normal number
- Spermatocytes present/normal number
- Spermatogonia present/normal number
- Different stages of spermatogenic cycle present

EPIDIDYMIS (RIGHT):

- Interstitial mononuclear cell aggregation, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29308 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

PROSTATE:

- Epithelial cell atrophy, grade 2
- Interstitial mononuclear cell aggregation, grade 1

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
- Round spermatids (steps 1-9) present/normal number
- Spermatocytes present/normal number
- Spermatogonia present/normal number
- Different stages of spermatogenic cycle present
- Degeneration of germinal epithelium, focal, below capsule, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29309 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 123
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

PITUITARY GLAND:

-Vacuolated cells, grade 1

PROSTATE:

-Epithelial cell atrophy, grade 1

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Degenerated/necrotic cells sloughed in lumen, grade 1

-Seminiferous tubules lined by Sertoli cells only, focal,
grade 1

-Vacuolated sertoli cells, focal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29310 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 123
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

PROSTATE:

-Subacute prostatitis, grade 3

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Vacuolated seminiferous tubules, focal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29311 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 25.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 25.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

PROSTATE:

-Epithelial cell atrophy, grade 3

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29312 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 25.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 25.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 2

PITUITARY GLAND:

-Vacuolated cells, grade 1

PROSTATE:

-Subacute prostatitis, grade 4

SEMINAL VESICLES+ COAGULATING GLANDS:

Organ examined, no pathologic findings noted

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Degenerated/necrotic cells sloughed in lumen, grade 1

EPIDIDYMIS (RIGHT):

-Interstitial mononuclear cell aggregation, grade 1

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29313 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 25.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 25.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 2

PITUITARY GLAND:

-Vacuolated cells, grade 1

PROSTATE:

-Interstitial mononuclear cell aggregation, grade 1

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Degenerated/necrotic cells sloughed in lumen, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29314 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 25.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 25.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

SPLEEN:

01: ENLARGED.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
unilateral, grade 1

PITUITARY GLAND:

-Vacuolated cells, grade 2

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

SPLEEN:

-Lymphoid cell hyperplasia, grade 2

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29315 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 25.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 25.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

KIDNEYS:

01: RIGHT: DILATED PELVIS.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
unilateral, grade 1

PITUITARY GLAND:

-Vacuolated cells, grade 1

PROSTATE:

-Granulocyte infiltration, focal, grade 1

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Vacuolated seminiferous tubules, focal, grade 1

KIDNEYS:

-Dilated pelvis, unilateral, grade 3

This finding corresponds to necropsy observation no: 01.

-Tubular basophilia, unilateral, grade 2

-Peritubular fibrosis, unilateral, grade 2

-Interstitial mononuclear cell aggregation, unilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29316 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

- Interstitial mononuclear cell aggregation, unilateral, grade 1
- Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
- Round spermatids (steps 1-9) present/normal number
- Spermatocytes present/normal number
- Spermatogonia present/normal number
- Different stages of spermatogenic cycle present

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29317 SEX : MALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

- Interstitial mononuclear cell aggregation, focal, unilateral, grade 1
- Sinusoidal ectasia sometimes with blood extravasation, bilateral, grade 1

PITUITARY GLAND:

- Vacuolated cells, grade 1

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
- Round spermatids (steps 1-9) present/normal number
- Spermatocytes present/normal number
- Spermatogonia present/normal number
- Different stages of spermatogenic cycle present
- Degenerated/necrotic cells sloughed in lumen, grade 1
- Seminiferous tubules lined by Sertoli cells only, grade 1
- Vacuolated seminiferous tubules, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29318 SEX : MALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number
-Round spermatids (steps 1-9) present/normal number
-Spermatocytes present/normal number
-Spermatogonia present/normal number
-Different stages of spermatogenic cycle present
-Seminiferous tubules lined by Sertoli cells only, focal,
grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29319 SEX : MALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

PROSTATE:

-Epithelial cell atrophy, grade 2

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Seminiferous tubules lined by Sertoli cells only, focal,
grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29320 SEX : MALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

THYMUS:

01: FOCI REDDISH/PURPLISH, SEVERAL, UP TO 0.1 CM IN DIAMETER.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

PITUITARY GLAND:

-Vacuolated cells, grade 1

PROSTATE:

-Epithelial cell atrophy, grade 1
-Interstitial mononuclear cell aggregation, grade 1

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number
-Round spermatids (steps 1-9) present/normal number
-Spermatocytes present/normal number
-Spermatogonia present/normal number
-Different stages of spermatogenic cycle present

THYMUS:

-Capillary hemorrhage, grade 3

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29321 SEX : MALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

PROSTATE:

-Epithelial cell atrophy, grade 1

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Degenerated/necrotic cells sloughed in lumen, grade 1

-Seminiferous tubules lined by Sertoli cells only, focal,
grade 1

-Vacuolated seminiferous tubules, focal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29322 SEX : MALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 123
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

PITUITARY GLAND:

-Vacuolated cells, grade 1

PROSTATE:

-Subacute prostatitis, grade 2

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Vacuolated seminiferous tubules, focal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29323 SEX : MALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 123
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

PITUITARY GLAND:

-Vacuolated cells, grade 2

PROSTATE:

-Epithelial cell atrophy, grade 1

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Vacuolated seminiferous tubules, focal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29324 SEX : MALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 123
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

PROSTATE:

-Epithelial cell atrophy, grade 1

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Degenerated/necrotic cells sloughed in lumen, grade 1

-Seminiferous tubules lined by Sertoli cells only, focal,
grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29325 SEX : MALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 123
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

- Accessory adrenal cortex, unilateral
- Sinusoidal ectasia sometimes with blood extravasation, bilateral, grade 2

PROSTATE:

- Epithelial cell atrophy, grade 3
- Interstitial mononuclear cell aggregation, grade 1

SEMINAL VESICLES+ COAGULATING GLANDS:

- Interstitial mononuclear cell aggregation, unilateral, grade 1
coagulating gland

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
- Round spermatids (steps 1-9) present/normal number
- Spermatocytes present/normal number
- Spermatogonia present/normal number
- Different stages of spermatogenic cycle present
- Degenerated/necrotic cells sloughed in lumen, grade 1
- Seminiferous tubules lined by Sertoli cells only, focal, grade 1
- Vacuolated seminiferous tubules, focal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29701 SEX : FEMALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 17.11.03
DAYS ON TEST : 118
DATE OF NECROPSY : 17.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

OVARIES:

-Diestrus, bilateral

OVIDUCTS:

Only one of paired organs examined/present

UTERUS:

-Diestrus

VAGINA:

-Diestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29702 SEX : FEMALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 17.11.03
DAYS ON TEST : 118
DATE OF NECROPSY : 17.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

UTERUS:

01: BOTH HORNS: SEROUS CONTENTS.

ADIPOSE TISSUE:

01: OVARIAN REGION, NODULE YELLOWISH, APPROX 0.5 CM IN
DIAMETER, (A).

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 2

OVARIES:

-Proestrus, bilateral

UTERUS:

-Proestrus, residual morphology of pseudo-pregnancy

This finding corresponds to necropsy observation no: 01.

-Dilated lumen, both horns, grade 2

VAGINA:

-Proestrus, residual mucification/previous pseudo-pregnancy

ADIPOSE TISSUE:

-Fat necrosis, grade 2

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29703 SEX : FEMALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 03.11.03
DAYS ON TEST : 104
DATE OF NECROPSY : 03.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

ILEUM (+ PEYERS PATCHES):
01: MUCOSA: WHITISH COLOR.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:
-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1
OVARIES:
-Diestrus, bilateral
UTERUS:
poor quality
VAGINA:
-Diestrus
ILEUM (+ PEYERS PATCHES):
Nothing abnormal discovered corresponding with the necropsy
observation no.01.
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29704 SEX : FEMALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 12.11.03
DAYS ON TEST : 113
DATE OF NECROPSY : 12.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

OVARIES:

-Diestrus, bilateral

UTERUS:

-Diestrus

VAGINA:

-Diestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29705 SEX : FEMALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 17.11.03
DAYS ON TEST : 117
DATE OF NECROPSY : 17.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
unilateral, grade 1

OVARIES:

-Metestrus, bilateral

UTERUS:

-Metestrus

-Yellowish pigment laden macrophages, both horns, grade 2
with perivascular hyalinosis

VAGINA:

-Metestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29706 SEX : FEMALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 17.11.03
DAYS ON TEST : 117
DATE OF NECROPSY : 17.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

ADRENAL GLANDS:

01: LEFT: FOCUS BROWNISH/BLACKISH, APPROX 0.2 CM IN DIAMETER.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

Nothing abnormal discovered corresponding with the necropsy
observation no.01.

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

PITUITARY GLAND:

-Cyst(s), pars intermedia, grade 1

UTERUS:

-Yellowish pigment laden macrophages, 1/2 horns, grade 2

VAGINA:

-Epithelial cell hyperplasia, grade 3

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29707 SEX : FEMALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 27.10.03
DAYS ON TEST : 96
DATE OF NECROPSY : 27.10.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

UTERUS:

poor quality

VAGINA:

-Mucification vaginal epithelium, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29708 SEX : FEMALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 14.11.03
DAYS ON TEST : 114
DATE OF NECROPSY : 14.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

OVARIES:

-Metestrus, bilateral

UTERUS:

-Metestrus

VAGINA:

-Metestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29709 SEX : FEMALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 13.11.03
DAYS ON TEST : 112
DATE OF NECROPSY : 13.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
unilateral, grade 1

OVARIES:

-Diestrus, bilateral

UTERUS:

-Diestrus

-Yellowish pigment laden macrophages, 1/2 horns, grade 3

VAGINA:

-Diestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29710 SEX : FEMALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 13.11.03
DAYS ON TEST : 112
DATE OF NECROPSY : 13.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 2

OVARIES:

-Proestrus, bilateral

UTERUS:

-Proestrus
-Dilated lumen, both horns, grade 2

VAGINA:

-Proestrus, residual mucification/previous pseudo-pregnancy

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29711 SEX : FEMALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 13.11.03
DAYS ON TEST : 112
DATE OF NECROPSY : 13.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

- Sinusoidal ectasia sometimes with blood extravasation,
unilateral, grade 1
- Lipomatosis, focal, unilateral, grade 1

OVARIES:

- Metestrus, bilateral

UTERUS:

- Metestrus
- Yellowish pigment laden macrophages, 1/2 horns, grade 1

VAGINA:

- Metestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29712 SEX : FEMALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 27.10.03
DAYS ON TEST : 95
DATE OF NECROPSY : 27.10.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 2

OVARIES:

-Metestrus, bilateral

VAGINA:

-Metestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29713 SEX : FEMALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 17.11.03
DAYS ON TEST : 116
DATE OF NECROPSY : 17.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

OVARIES:

-Proestrus, bilateral

OVIDUCTS:

Only one of paired organs examined/present

UTERUS:

-Proestrus, morphology of previous pseudo-pregnancy

-Dilated lumen, grade 1

VAGINA:

-Proestrus, residual mucification/previous pseudo-pregnancy

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29714 SEX : FEMALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 21.11.03
DAYS ON TEST : 120
DATE OF NECROPSY : 21.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
unilateral, grade 1

OVARIES:

-Diestrus, bilateral

UTERUS:

-Diestrus

-Yellowish pigment laden macrophages, 1/2 horns, grade 2

VAGINA:

-Diestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29715 SEX : FEMALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 18.11.03
DAYS ON TEST : 117
DATE OF NECROPSY : 18.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

OVARIES:

-Estrus, bilateral

UTERUS:

-Estrus

VAGINA:

-Estrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29716 SEX : FEMALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 17.11.03
DAYS ON TEST : 116
DATE OF NECROPSY : 17.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

OVARIES:

-Diestrus, bilateral

OVIDUCTS:

Only one of paired organs examined/present

UTERUS:

-Diestrus

-Yellowish pigment laden macrophages, both horns, grade 2
sometimes with hyalinosis

VAGINA:

-Diestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29717 SEX : FEMALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 18.11.03
DAYS ON TEST : 116
DATE OF NECROPSY : 18.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

OVARIES:

-Proestrus, bilateral

UTERUS:

-Proestrus

-Yellowish pigment laden macrophages, grade 1
sometimes with perivascular hyalinosis

-Dilated lumen, 1/2 horns, grade 1

VAGINA:

-Proestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29718 SEX : FEMALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 12.11.03
DAYS ON TEST : 110
DATE OF NECROPSY : 12.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 2

OVARIES:

-Diestrus, bilateral

UTERUS:

-Diestrus

-Yellowish pigment laden macrophages, both horns, grade 3

VAGINA:

-Diestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29719 SEX : FEMALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 14.11.03
DAYS ON TEST : 112
DATE OF NECROPSY : 14.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 2

PITUITARY GLAND:

-Developmental cyst(s), multiple

OVARIES:

-Metestrus, bilateral

OVIDUCTS:

Organ examined, no pathologic findings noted

UTERUS:

-Metestrus

VAGINA:

-Metestrus

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29720 SEX : FEMALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 22.10.03
DAYS ON TEST : 89
DATE OF NECROPSY : 22.10.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 2

UTERUS:

-Morphology of pregnancy

VAGINA:

-Mucification vaginal epithelium, grade 3

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29721 SEX : FEMALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 14.11.03
DAYS ON TEST : 112
DATE OF NECROPSY : 14.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
unilateral, grade 2

OVARIES:

-Metestrus, bilateral

UTERUS:

-Metestrus

-Yellowish pigment laden macrophages, grade 1
with perivascular hyalinosis

-Mineralization, 1/2 horns, grade 1

VAGINA:

-Metestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29722 SEX : FEMALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 14.11.03
DAYS ON TEST : 111
DATE OF NECROPSY : 14.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

UTERUS:

01: BOTH HORNS: SEROUS CONTENTS.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

OVARIES:

-Proestrus, bilateral

UTERUS:

-Proestrus

This finding corresponds to necropsy observation no: 01.

-Dilated lumen, both horns, grade 3

VAGINA:

-Proestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29723 SEX : FEMALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 14.11.03
DAYS ON TEST : 111
DATE OF NECROPSY : 14.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

OVARIES:

-Metestrus, bilateral

OVIDUCTS:

Only one of paired organs examined/present

UTERUS:

-Metestrus

VAGINA:

-Metestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29724 SEX : FEMALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 17.11.03
DAYS ON TEST : 114
DATE OF NECROPSY : 17.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 2

OVARIES:

-Diestrus, bilateral

UTERUS:

-Diestrus

VAGINA:

-Diestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 1, 0mg/kg/d.F1

* ANIMAL NUMBER : B29725 SEX : FEMALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 17.11.03
DAYS ON TEST : 114
DATE OF NECROPSY : 17.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

OVARIES:

-Estrus, bilateral

UTERUS:

-Estrus

-Yellowish pigment laden macrophages, 1/2 horns, grade 2

VAGINA:

-Estrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

ANIMAL HEADING DATA

DOSE GROUP : 2, 250mg/kg/d.F1

| ANIMAL NUMBER | SEX M/F | DEFINED AND FINAL STATE OF NECROPSY | FINAL NECROPSY | TEST DAYS | FIRST AND LAST DAY UNDER TEST | DATE OF NECROPSY |
|------------------|------------|--|-------------------|--------------|----------------------------------|---------------------|
| B29326 | M | K0 | K0 | 125 | 23-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29327 | M | K0 | K0 | 125 | 23-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29328 | M | K0 | K0 | 125 | 23-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29329 | M | K0 | K0 | 125 | 23-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29330 | M | K0 | K0 | 125 | 23-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29331 | M | K0 | K0 | 125 | 23-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29332 | M | K0 | K0 | 125 | 23-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29333 | M | K0 | K0 | 124 | 24-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29334 | M | K0 | K0 | 124 | 24-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29335 | M | K0 | K0 | 124 | 24-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29336 | M | K0 | K0 | 125 | 24-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29337 | M | K0 | K0 | 125 | 24-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29338 | M | K0 | K0 | 125 | 24-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29339 | M | K0 | K0 | 125 | 24-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29340 | M | K0 | K0 | 124 | 25-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29341 | M | K0 | K0 | 125 | 25-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29342 | M | K0 | K0 | 125 | 25-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29343 | M | K0 | K0 | 125 | 25-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29344 | M | K0 | K0 | 125 | 25-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29345 | M | K0 | K0 | 125 | 25-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29346 | M | K0 | K0 | 124 | 26-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29347 | M | K0 | K0 | 124 | 26-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29348 | M | K0 | K0 | 123 | 27-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29349 | M | K0 | K0 | 123 | 27-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29350 | M | K0 | K0 | 123 | 27-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29726 | F | K0 | K0 | 118 | 23-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29727 | F | K0 | K0 | 119 | 23-JUL-03 18-NOV-03 | 18-NOV-03 |
| B29728 | F | K0 | K0 | 115 | 23-JUL-03 14-NOV-03 | 14-NOV-03 |
| B29729 | F | K0 | K0 | 113 | 23-JUL-03 12-NOV-03 | 12-NOV-03 |
| B29730 | F | K0 | K0 | 97 | 23-JUL-03 27-OCT-03 | 27-OCT-03 |
| B29731 | F | K0 | K0 | 114 | 23-JUL-03 13-NOV-03 | 13-NOV-03 |
| B29732 | F | K0 | K0 | 125 | 23-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29733 | F | K0 | K0 | 114 | 24-JUL-03 14-NOV-03 | 14-NOV-03 |
| B29734 | F | K0 | K0 | 125 | 24-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29735 | F | K0 | K0 | 118 | 24-JUL-03 18-NOV-03 | 18-NOV-03 |
| B29736 | F | K0 | K0 | 113 | 24-JUL-03 13-NOV-03 | 13-NOV-03 |
| B29737 | F | K0 | K0 | 96 | 24-JUL-03 27-OCT-03 | 27-OCT-03 |
| B29738 | F | K0 | K0 | 99 | 24-JUL-03 30-OCT-03 | 30-OCT-03 |
| B29739 | F | K0 | +2 | 96 | 24-JUL-03 27-OCT-03 | 27-OCT-03 |
| B29740 | F | K0 | K0 | 113 | 25-JUL-03 14-NOV-03 | 14-NOV-03 |

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

ANIMAL HEADING DATA

DOSE GROUP : 2, 250mg/kg/d.F1

| ANIMAL NUMBER | SEX M/F | DEFINED AND FINAL STATE OF NECROPSY | TEST DAYS | FIRST AND LAST DAY UNDER TEST | DATE OF NECROPSY | |
|------------------|------------|--|--------------|----------------------------------|---------------------|-----------|
| B29741 | F | K0 | K0 | 117 | 25-JUL-03 18-NOV-03 | 18-NOV-03 |
| B29742 | F | K0 | K0 | 112 | 25-JUL-03 13-NOV-03 | 13-NOV-03 |
| B29743 | F | K0 | K0 | 112 | 25-JUL-03 13-NOV-03 | 13-NOV-03 |
| B29744 | F | K0 | K0 | 117 | 25-JUL-03 18-NOV-03 | 18-NOV-03 |
| B29745 | F | K0 | K0 | 117 | 25-JUL-03 18-NOV-03 | 18-NOV-03 |
| B29746 | F | K0 | K0 | 89 | 26-JUL-03 22-OCT-03 | 22-OCT-03 |
| B29747 | F | K0 | K0 | 116 | 26-JUL-03 18-NOV-03 | 18-NOV-03 |
| B29748 | F | K0 | K0 | 110 | 27-JUL-03 13-NOV-03 | 13-NOV-03 |
| B29749 | F | K0 | K0 | 110 | 27-JUL-03 13-NOV-03 | 13-NOV-03 |
| B29750 | F | K0 | K0 | 114 | 27-JUL-03 17-NOV-03 | 17-NOV-03 |

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CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29326 SEX : MALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29327 SEX : MALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Seminiferous tubules lined by Sertoli cells only, grade 1
along albuginea
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29328 SEX : MALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

THYMUS:

01: RIGHT LOBE: REDUCED IN SIZE.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Degenerated/necrotic cells sloughed in lumen, focal, grade 1
 - Vacuolated seminiferous tubules, focal, grade 1
 - Degeneration of germinal epithelium, focal, grade 1
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29329 SEX : MALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Degenerated/necrotic cells sloughed in lumen, grade 2
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29330 SEX : MALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Vacuolated seminiferous tubules, focal, grade 1
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29331 SEX : MALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29332 SEX : MALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29333 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

TESTES:

01: SOFT, REDUCED IN SIZE.

EPIDIDYMIDES:

01: REDUCED IN SIZE.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

PROSTATE:

-Epithelial cell atrophy, grade 3

TESTIS, RIGHT:

-Reduced number of tailed spermatids, grade 4

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Reduced round spermatids, grade 4

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Spermatocytes reduced in number, grade 4

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Spermatogonia Reduced, grade 4

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Different stages of cycle disturbed, grade 4

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Seminiferous tubules lined by Sertoli cells only, grade 4

This finding corresponds to necropsy observation no.: 01

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 2, 250mg/kg/d.F1

CONT./FF. ANIMAL NO. : B29333
.....

in the TESTES.

-Spermatic granuloma, grade 2

EPIDIDYMIS (RIGHT):

-Oligospermia, grade 4

This finding corresponds to necropsy observation no.: 01
in the EPIDIDYMIDES.

TESTES:

Organ not examined

For diagnosis of necropsy observation no. 01 see under:

TESTIS, RIGHT.

EPIDIDYMIDES:

Organ not examined

For diagnosis of necropsy observation no. 01 see under:

EPIDIDYMIS (RIGHT).

SEMINAL VESICLE:

Organ examined, no pathologic findings noted

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29334 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Degenerated/necrotic cells sloughed in lumen, focal, grade 1
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29335 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29336 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 25.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 25.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29337 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 25.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 25.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Seminiferous tubules lined by Sertoli cells only, focal,
grade 1
under albuginea
 - Vacuolated seminiferous tubules, focal, grade 1
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29338 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 25.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 25.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29339 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 25.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 25.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Degenerated/necrotic cells sloughed in lumen, grade 1
 - Seminiferous tubules lined by Sertoli cells only, focal, grade 1
beneath albuginea
 - Vacuolated seminiferous tubules, focal, grade 1
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29340 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 25.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 25.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

TESTES:

01: RIGHT: TRANSLUCENT ASPECT.

EPIDIDYMIDES:

01: RIGHT: REDUCED IN SIZE.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

-Reduced number of tailed spermatids, grade 5

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Reduced round spermatids, grade 5

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Spermatocytes reduced in number, grade 5

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Spermatogonia Reduced, grade 5

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Different stages of cycle disturbed, grade 5

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Seminiferous tubules lined by Sertoli cells only, grade 5

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Vacuolated sertoli cells, grade 3

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 2, 250mg/kg/d.F1

CONT./FF. ANIMAL NO. : B29340
.....

TESTES:

Organ not examined

For diagnosis of necropsy observation no. 01 see under:

TESTIS, RIGHT.

EPIDIDYMIDES:

Tissue with necropsy observation no.01 not submitted for
microscopic examination.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29341 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

ADRENAL GLANDS:

01: RIGHT: REDUCED IN SIZE.

TESTES:

01: LEFT: ENLARGED.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

Organ examined, no pathologic findings noted

Nothing abnormal discovered corresponding with the necropsy
observation no.01.

PROSTATE:

-Epithelial cell atrophy, grade 4

SEMINAL VESICLES+ COAGULATING GLANDS:

Organ examined, no pathologic findings noted

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

EPIDIDYMIS (RIGHT):

Organ examined, no pathologic findings noted

TESTIS, LEFT:

Tissue not present for histologic examination

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

CONT./FF. ANIMAL NO. : B29341
.....

TESTES:

Organ not examined

Tissue with necropsy observation no.01 not submitted for
microscopic examination.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29342 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29343 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Vacuolated seminiferous tubules, focal, grade 1
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29344 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29345 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Multinucleated Giant Cells, focal, grade 1
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29346 SEX : MALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

KIDNEYS:

01: IRREGULAR COLOR.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29347 SEX : MALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29348 SEX : MALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 123
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Seminiferous tubules lined by Sertoli cells only, focal,
grade 1
beneath albuginea
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29349 SEX : MALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 123
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29350 SEX : MALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 123
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

TESTES:

01: REDUCED IN SIZE.

EPIDIDYMIDES:

01: REDUCED IN SIZE, TRANSLUCENT ASPECT.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

PROSTATE:

- Epithelial cell atrophy, grade 1
- Interstitial mononuclear cell aggregation, grade 2
- Subacute prostatitis, grade 2

SEMINAL VESICLES+ COAGULATING GLANDS:

Organ examined, no pathologic findings noted

TESTIS, RIGHT:

- Reduced number of tailed spermatids, grade 5
This finding corresponds to necropsy observation no.: 01
in the TESTES.
- Reduced round spermatids, grade 5
This finding corresponds to necropsy observation no.: 01
in the TESTES.
- Spermatocytes reduced in number, grade 5
This finding corresponds to necropsy observation no.: 01
in the TESTES.
- Spermatogonia Reduced, grade 5
This finding corresponds to necropsy observation no.: 01
in the TESTES.
- Different stages of cycle disturbed, grade 5

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 2, 250mg/kg/d.F1

CONT./FF. ANIMAL NO. : B29350
.....

This finding corresponds to necropsy observation no.: 01
in the TESTES.
-Seminiferous tubules lined by Sertoli cells only, grade 5
This finding corresponds to necropsy observation no.: 01
in the TESTES.
-Vacuolated sertoli cells, grade 3
EPIDIDYMIS (RIGHT):
-Oligospermia, grade 4
This finding corresponds to necropsy observation no.: 01
in the EPIDIDYMIDES.
TESTES:
Organ not examined
For diagnosis of necropsy observation no. 01 see under:
TESTIS, RIGHT.
EPIDIDYMIDES:
Organ not examined
For diagnosis of necropsy observation no. 01 see under:
EPIDIDYMIS (RIGHT).

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29727 SEX : FEMALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 18.11.03
DAYS ON TEST : 119
DATE OF NECROPSY : 18.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

UTERUS:

01: BOTH HORNS: SEROUS CONTENTS.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29738 SEX : FEMALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 30.10.03
DAYS ON TEST : 99
DATE OF NECROPSY : 30.10.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

THYROID GLANDS:

01: LEFT: ENLARGED.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

OVARIES:

Only one of paired organs examined/present

UTERUS:

-Morphology of pregnancy, at level of one horn
characterized by marked vascular changes in uterine wall

VAGINA:

-Mucification vaginal epithelium, grade 2
-Epithelial cell hyperplasia, covered by mucification, grade 2

THYROID GLANDS:

Nothing abnormal discovered corresponding with the necropsy
observation no.01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29739 SEX : FEMALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 27.10.03
DAYS ON TEST : 96
DATE OF NECROPSY : 27.10.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : SACRIFICED MORIBUND
.....

* NECROPSY FINDINGS

ILEUM (+ PEYERS PATCHES):
01: DISTENDED WITH GAS.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

OVARIES:

-Proestrus, bilateral

OVIDUCTS:

Only one of paired organs examined/present

UTERUS:

-Proestrus

-Yellowish pigment laden macrophages, both horns, grade 2
sometimes with hyalinosis

-Dilated lumen, both horns, grade 2

VAGINA:

-Proestrus

ILEUM (+ PEYERS PATCHES):

Nothing abnormal discovered corresponding with the necropsy
observation no.01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29746 SEX : FEMALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 22.10.03
DAYS ON TEST : 89
DATE OF NECROPSY : 22.10.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

OVARIES:

-Estrus, bilateral

UTERUS:

poor quality

VAGINA:

-Estrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 2, 250mg/kg/d.F1

* ANIMAL NUMBER : B29747 SEX : FEMALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 18.11.03
DAYS ON TEST : 116
DATE OF NECROPSY : 18.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

UTERUS:

01: BOTH HORNS: SEROUS CONTENTS.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

- ALL OTHER ANIMALS IN DOSE GROUP WITHOUT PATHOLOGICAL FINDINGS -

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

ANIMAL HEADING DATA

DOSE GROUP : 3, 500mg/kg/d.F1

| ANIMAL NUMBER | SEX M/F | DEFINED AND FINAL STATE OF NECROPSY | FINAL NECROPSY | TEST DAYS | FIRST AND LAST DAY UNDER TEST | DATE OF NECROPSY |
|------------------|------------|--|-------------------|--------------|----------------------------------|---------------------|
| B29351 | M | K0 | K0 | 125 | 23-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29352 | M | K0 | K0 | 125 | 23-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29353 | M | K0 | K0 | 125 | 23-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29354 | M | K0 | K0 | 125 | 23-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29355 | M | K0 | K0 | 125 | 23-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29356 | M | K0 | K0 | 125 | 23-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29357 | M | K0 | K0 | 124 | 24-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29358 | M | K0 | K0 | 124 | 24-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29359 | M | K0 | K0 | 124 | 24-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29360 | M | K0 | K0 | 124 | 24-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29361 | M | K0 | K0 | 125 | 24-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29362 | M | K0 | K0 | 125 | 24-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29363 | M | K0 | K0 | 125 | 24-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29364 | M | K0 | K0 | 125 | 24-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29365 | M | K0 | K0 | 125 | 24-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29366 | M | K0 | K0 | 125 | 25-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29367 | M | K0 | K0 | 125 | 25-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29368 | M | K0 | K0 | 125 | 25-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29369 | M | K0 | K0 | 125 | 25-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29370 | M | K0 | K0 | 124 | 26-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29371 | M | K0 | K0 | 124 | 26-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29372 | M | K0 | K0 | 124 | 26-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29373 | M | K0 | K0 | 123 | 27-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29374 | M | K0 | K0 | 123 | 27-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29375 | M | K0 | +1 | 93 | 27-JUL-03 27-OCT-03 | 27-OCT-03 |
| B29751 | F | K0 | K0 | 118 | 23-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29752 | F | K0 | K0 | 115 | 23-JUL-03 14-NOV-03 | 14-NOV-03 |
| B29753 | F | K0 | K0 | 115 | 23-JUL-03 14-NOV-03 | 14-NOV-03 |
| B29754 | F | K0 | K0 | 119 | 23-JUL-03 18-NOV-03 | 18-NOV-03 |
| B29755 | F | K0 | K0 | 114 | 23-JUL-03 13-NOV-03 | 13-NOV-03 |
| B29756 | F | K0 | K0 | 118 | 23-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29757 | F | K0 | K0 | 117 | 24-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29758 | F | K0 | K0 | 117 | 24-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29759 | F | K0 | K0 | 117 | 24-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29760 | F | K0 | K0 | 113 | 24-JUL-03 13-NOV-03 | 13-NOV-03 |
| B29761 | F | K0 | K0 | 99 | 24-JUL-03 30-OCT-03 | 30-OCT-03 |
| B29762 | F | K0 | K0 | 96 | 24-JUL-03 27-OCT-03 | 27-OCT-03 |
| B29763 | F | K0 | K0 | 117 | 24-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29764 | F | K0 | K0 | 117 | 24-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29765 | F | K0 | K0 | 113 | 24-JUL-03 13-NOV-03 | 13-NOV-03 |

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

ANIMAL HEADING DATA

DOSE GROUP : 3, 500mg/kg/d.F1

| ANIMAL NUMBER | SEX M/F | DEFINED AND FINAL STATE OF NECROPSY | TEST DAYS | FIRST AND LAST DAY UNDER TEST | DATE OF NECROPSY | |
|------------------|------------|--|--------------|----------------------------------|---------------------|-----------|
| B29766 | F | K0 | K0 | 111 | 25-JUL-03 12-NOV-03 | 12-NOV-03 |
| B29767 | F | K0 | K0 | 117 | 25-JUL-03 18-NOV-03 | 18-NOV-03 |
| B29768 | F | K0 | K0 | 113 | 25-JUL-03 14-NOV-03 | 14-NOV-03 |
| B29769 | F | K0 | K0 | 112 | 25-JUL-03 13-NOV-03 | 13-NOV-03 |
| B29770 | F | K0 | K0 | 112 | 26-JUL-03 14-NOV-03 | 14-NOV-03 |
| B29771 | F | K0 | K0 | 115 | 26-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29772 | F | K0 | K0 | 111 | 26-JUL-03 13-NOV-03 | 13-NOV-03 |
| B29773 | F | K0 | K0 | 93 | 27-JUL-03 27-OCT-03 | 27-OCT-03 |
| B29774 | F | K0 | K0 | 111 | 27-JUL-03 14-NOV-03 | 14-NOV-03 |
| B29775 | F | K0 | K0 | 110 | 27-JUL-03 13-NOV-03 | 13-NOV-03 |

.....

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29351 SEX : MALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29352 SEX : MALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Degenerated/necrotic cells sloughed in lumen, focal, grade 1
 - Vacuolated seminiferous tubules, focal, grade 1
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29353 SEX : MALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Degenerated/necrotic cells sloughed in lumen, focal, grade 1
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29354 SEX : MALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

KIDNEYS:

01: PALENESS.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29355 SEX : MALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Seminiferous tubules lined by Sertoli cells only, focal,
grade 1
beneath albuginea
 - Vacuolated sertoli cells, focal, grade 1
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29356 SEX : MALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Degenerated/necrotic cells sloughed in lumen, grade 2
 - Seminiferous tubules lined by Sertoli cells only, grade 1
beneath albuginea
 - Retained spermatids (stage 19 within tubules of stage>IX),
grade 1
in a few tubules of stage X
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29357 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

TESTES:

01: REDUCED IN SIZE, SOFT.

EPIDIDYMIDES:

01: REDUCED IN SIZE.

KIDNEYS:

01: PALENESS.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

PROSTATE:

-Interstitial mononuclear cell aggregation, grade 2

-Acute Prostatitis, focal, grade 2

SEMINAL VESICLES+ COAGULATING GLANDS:

Organ examined, no pathologic findings noted

TESTIS, RIGHT:

-Reduced number of tailed spermatids, grade 5

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Reduced round spermatids, grade 5

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Spermatocytes reduced in number, grade 5

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Spermatogonia Reduced, grade 5

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Different stages of cycle disturbed, grade 5

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 3, 500mg/kg/d.F1

CONT./FF. ANIMAL NO. : B29357
.....

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Seminiferous tubules lined by Sertoli cells only, grade 5
This finding corresponds to necropsy observation no.: 01
in the TESTES.

EPIDIDYMIS (RIGHT):

-Oligospermia, grade 3

This finding corresponds to necropsy observation no.: 01
in the EPIDIDYMIDES.

-Exfoliated spermatids sloughed in epididymal ducts, grade 3
This finding corresponds to necropsy observation no.: 01
in the EPIDIDYMIDES.

TESTES:

Organ not examined

For diagnosis of necropsy observation no. 01 see under:
TESTIS, RIGHT.

EPIDIDYMIDES:

Organ not examined

For diagnosis of necropsy observation no. 01 see under:
EPIDIDYMIS (RIGHT).

KIDNEYS:

-Tubular basophilia, bilateral, grade 3

This finding corresponds to necropsy observation no: 01.

-Peritubular fibrosis, bilateral, grade 3

This finding corresponds to necropsy observation no: 01.

-Tubular dilatation, bilateral, grade 2

This finding corresponds to necropsy observation no: 01.

-Acidophilic globules in cortical tubular epithelium, bilateral,
grade 4

This finding corresponds to necropsy observation no: 01.

-Degenerated/necrotic cells sloughed in tubular lumens,
bilateral, grade 3

This finding corresponds to necropsy observation no: 01.

-Interstitial mononuclear cell aggregation, bilateral, grade 2

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29358 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Degenerated/necrotic cells sloughed in lumen, grade 1
 - Seminiferous tubules lined by Sertoli cells only, focal, grade 1
beneath albuginea
 - Vacuolated sertoli cells, focal, grade 1
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29359 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

KIDNEYS:

01: GREY/GREEN COLOR.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29360 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29361 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 25.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 25.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29362 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 25.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 25.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Degenerated/necrotic cells sloughed in lumen, grade 1
 - Seminiferous tubules lined by Sertoli cells only, focal, grade 1
 - Vacuolated seminiferous tubules, focal, grade 1
 - Vacuolated sertoli cells, focal, grade 1
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29363 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 25.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 25.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

KIDNEYS:

01: RIGHT: DILATED PELVIS.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29364 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 25.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 25.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29365 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 25.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 25.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29366 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Degenerated/necrotic cells sloughed in lumen, grade 2
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29367 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Seminiferous tubules lined by Sertoli cells only, focal,
grade 1
beneath albuginea
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29368 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

PROSTATE:

-Interstitial mononuclear cell aggregation, grade 1

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Seminiferous tubules lined by Sertoli cells only, focal,
grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29369 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

KIDNEYS:

01: PALENESS.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29370 SEX : MALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

KIDNEYS:

01: IRREGULAR COLOR.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29371 SEX : MALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Vacuolated seminiferous tubules, focal, grade 1
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29372 SEX : MALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

ADIPOSE TISSUE:

01: PANCREATIC REGION, NODULE REDDISH/PURPLISH, APPROX 0.4 CM
IN DIAMETER, (A).
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29373 SEX : MALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 123
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Degenerated/necrotic cells sloughed in lumen, grade 2
 - Seminiferous tubules lined by Sertoli cells only, focal,
grade 1
beneath albuginea
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29374 SEX : MALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 123
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
 - Round spermatids (steps 1-9) present/normal number
 - Spermatocytes present/normal number
 - Spermatogonia present/normal number
 - Different stages of spermatogenic cycle present
 - Degenerated/necrotic cells sloughed in lumen, grade 1
grading does not include presence of desquamated cells in
lumen considered to be due to technical artifacts
 - Seminiferous tubules lined by Sertoli cells only, focal,
grade 1
beneath albuginea
 - Vacuolated seminiferous tubules, focal, grade 1
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29375 SEX : MALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 27.10.03
DAYS ON TEST : 93
DATE OF NECROPSY : 27.10.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : FOUND DEAD
.....

* NECROPSY FINDINGS

LUNGS (+ BRONCHI) :
01: DILATATION, FOAMY CONTENTS.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29757 SEX : FEMALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 17.11.03
DAYS ON TEST : 117
DATE OF NECROPSY : 17.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

UTERUS:
01: BOTH HORNS: SEROUS CONTENTS.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29761 SEX : FEMALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 30.10.03
DAYS ON TEST : 99
DATE OF NECROPSY : 30.10.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

OVARIES:

-Diestrus, bilateral

UTERUS:

poor quality

VAGINA:

-Diestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29762 SEX : FEMALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 27.10.03
DAYS ON TEST : 96
DATE OF NECROPSY : 27.10.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

OVARIES:

-Diestrus, bilateral

OVIDUCTS:

Only one of paired organs examined/present

UTERUS:

poor quality

VAGINA:

-Diestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29771 SEX : FEMALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 17.11.03
DAYS ON TEST : 115
DATE OF NECROPSY : 17.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

UTERUS:
01: BOTH HORNS: SEROUS CONTENTS.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 3, 500mg/kg/d.F1

* ANIMAL NUMBER : B29773 SEX : FEMALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 27.10.03
DAYS ON TEST : 93
DATE OF NECROPSY : 27.10.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

UTERUS:

01: RIGHT HORN, BOTH HORNS: SEROUS CONTENTS.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

OVARIES:

-Proestrus, bilateral

UTERUS:

poor quality of the section
however dilatation of both horns is most probably related
to proestrus phase (see vagina)
Nothing abnormal discovered corresponding with the necropsy
observation no.01.

VAGINA:

-Proestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

- ALL OTHER ANIMALS IN DOSE GROUP WITHOUT PATHOLOGICAL FINDINGS -

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

ANIMAL HEADING DATA

DOSE GROUP : 4, 1000mg/kg/d.F1

| ANIMAL NUMBER | SEX M/F | DEFINED AND FINAL STATE OF NECROPSY | FINAL NECROPSY | TEST DAYS | FIRST AND LAST DAY UNDER TEST | DATE OF NECROPSY |
|------------------|------------|--|-------------------|--------------|----------------------------------|---------------------|
| B29376 | M | K0 | K0 | 125 | 23-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29377 | M | K0 | K0 | 125 | 23-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29378 | M | K0 | K0 | 125 | 23-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29379 | M | K0 | K0 | 124 | 24-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29380 | M | K0 | K0 | 124 | 24-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29381 | M | K0 | K0 | 124 | 24-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29382 | M | K0 | K0 | 124 | 24-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29383 | M | K0 | K0 | 124 | 24-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29384 | M | K0 | K0 | 124 | 24-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29385 | M | K0 | K0 | 123 | 25-JUL-03 24-NOV-03 | 24-NOV-03 |
| B29386 | M | K0 | K0 | 124 | 25-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29387 | M | K0 | K0 | 124 | 25-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29388 | M | K0 | K0 | 123 | 26-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29389 | M | K0 | K0 | 123 | 26-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29390 | M | K0 | K0 | 123 | 26-JUL-03 25-NOV-03 | 25-NOV-03 |
| B29391 | M | K0 | K0 | 124 | 26-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29392 | M | K0 | K0 | 124 | 26-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29393 | M | K0 | K0 | 124 | 26-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29394 | M | K0 | K0 | 124 | 26-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29395 | M | K0 | K0 | 124 | 26-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29396 | M | K0 | K0 | 124 | 26-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29397 | M | K0 | K0 | 124 | 26-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29398 | M | K0 | K0 | 123 | 27-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29399 | M | K0 | K0 | 123 | 27-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29400 | M | K0 | K0 | 123 | 27-JUL-03 26-NOV-03 | 26-NOV-03 |
| B29776 | F | K0 | K0 | 119 | 23-JUL-03 18-NOV-03 | 18-NOV-03 |
| B29777 | F | K0 | +1 | 47 | 23-JUL-03 07-SEP-03 | 07-SEP-03 |
| B29778 | F | K0 | K0 | 97 | 23-JUL-03 27-OCT-03 | 27-OCT-03 |
| B29779 | F | K0 | K0 | 114 | 24-JUL-03 14-NOV-03 | 14-NOV-03 |
| B29780 | F | K0 | K0 | 117 | 24-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29781 | F | K0 | K0 | 117 | 24-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29782 | F | K0 | K0 | 114 | 24-JUL-03 14-NOV-03 | 14-NOV-03 |
| B29783 | F | K0 | K0 | 117 | 24-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29784 | F | K0 | K0 | 114 | 24-JUL-03 14-NOV-03 | 14-NOV-03 |
| B29785 | F | K0 | K0 | 113 | 25-JUL-03 14-NOV-03 | 14-NOV-03 |
| B29786 | F | K0 | K0 | 90 | 25-JUL-03 22-OCT-03 | 22-OCT-03 |
| B29787 | F | K0 | K0 | 90 | 25-JUL-03 22-OCT-03 | 22-OCT-03 |
| B29788 | F | K0 | K0 | 112 | 26-JUL-03 14-NOV-03 | 14-NOV-03 |
| B29789 | F | K0 | K0 | 115 | 26-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29790 | F | K0 | K0 | 115 | 26-JUL-03 17-NOV-03 | 17-NOV-03 |

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

ANIMAL HEADING DATA

DOSE GROUP : 4, 1000mg/kg/d.F1

| ANIMAL NUMBER | SEX M/F | DEFINED AND FINAL STATE OF NECROPSY | TEST DAYS | FIRST AND LAST DAY UNDER TEST | DATE OF NECROPSY | |
|------------------|------------|--|--------------|----------------------------------|---------------------|-----------|
| B29791 | F | K0 | K0 | 111 | 26-JUL-03 13-NOV-03 | 13-NOV-03 |
| B29792 | F | K0 | K0 | 115 | 26-JUL-03 17-NOV-03 | 17-NOV-03 |
| B29793 | F | K0 | K0 | 111 | 26-JUL-03 13-NOV-03 | 13-NOV-03 |
| B29794 | F | K0 | K0 | 111 | 26-JUL-03 13-NOV-03 | 13-NOV-03 |
| B29795 | F | K0 | K0 | 112 | 26-JUL-03 14-NOV-03 | 14-NOV-03 |
| B29796 | F | K0 | K0 | 110 | 26-JUL-03 12-NOV-03 | 12-NOV-03 |
| B29797 | F | K0 | K0 | 111 | 26-JUL-03 13-NOV-03 | 13-NOV-03 |
| B29798 | F | K0 | K0 | 88 | 27-JUL-03 22-OCT-03 | 22-OCT-03 |
| B29799 | F | K0 | +2 | 93 | 27-JUL-03 27-OCT-03 | 27-OCT-03 |
| B29800 | F | K0 | K0 | 114 | 27-JUL-03 17-NOV-03 | 17-NOV-03 |

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CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29376 SEX : MALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Vacuolated cortical cell, bilateral, grade 2

PROSTATE:

-Interstitial mononuclear cell aggregation, multifocal, grade 1

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29377 SEX : MALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

- Accessory adrenal cortex, unilateral
- Sinusoidal ectasia sometimes with blood extravasation,
unilateral, grade 1

PROSTATE:

- Epithelial cell atrophy, grade 1
- Acute Prostatitis, focal, grade 1
- Subacute prostatitis, grade 2

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
- Round spermatids (steps 1-9) present/normal number
- Spermatocytes present/normal number
- Spermatogonia present/normal number
- Different stages of spermatogenic cycle present

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29378 SEX : MALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 125
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Lipomatosis, focal, unilateral, grade 1

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29379 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

- Accessory adrenal cortex, unilateral
- Sinusoidal ectasia sometimes with blood extravasation, unilateral, grade 1
- Vacuolated cortical cell, bilateral, grade 2

PITUITARY GLAND:

- Vacuolated cells, grade 1

PROSTATE:

- Hypersecretion, dorso-lateral part, grade 2
- Epithelial cell atrophy, grade 2

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
- Round spermatids (steps 1-9) present/normal number
- Spermatocytes present/normal number
- Spermatogonia present/normal number
- Different stages of spermatogenic cycle present
- Degenerated/necrotic cells sloughed in lumen, grade 1
- Seminiferous tubules lined by Sertoli cells only, focal, grade 1
- Vacuolated seminiferous tubules, focal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29380 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Interstitial mononuclear cell aggregation, bilateral, grade 1

PITUITARY GLAND:

-Vacuolated cells, grade 1

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Degeneration of germinal epithelium, focal, part of tubule,
grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29381 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

TESTES:

01: SOFT, REDUCED IN SIZE.

EPIDIDYMIDES:

01: REDUCED IN SIZE.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

Organ examined, no pathologic findings noted

PITUITARY GLAND:

-Vacuolated cells, grade 1

PROSTATE:

-Epithelial cell atrophy, grade 2

-Subacute prostatitis, grade 3

SEMINAL VESICLES+ COAGULATING GLANDS:

Organ examined, no pathologic findings noted

TESTIS, RIGHT:

-Reduced number of tailed spermatids, grade 5

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Reduced round spermatids, grade 5

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Spermatocytes reduced in number, grade 5

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Spermatogonia Reduced, grade 5

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 4, 1000mg/kg/d.F1

CONT./FF. ANIMAL NO. : B29381
.....

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Different stages of cycle disturbed, grade 5

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Seminiferous tubules lined by Sertoli cells only, grade 5

This finding corresponds to necropsy observation no.: 01
in the TESTES.

EPIDIDYMIS (RIGHT):

-Aspermia, grade 5

This finding corresponds to necropsy observation no.: 01
in the EPIDIDYMIDES.

TESTES:

Organ not examined

For diagnosis of necropsy observation no. 01 see under:
TESTIS, RIGHT.

EPIDIDYMIDES:

Organ not examined

For diagnosis of necropsy observation no. 01 see under:
EPIDIDYMIS (RIGHT).

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29382 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Interstitial mononuclear cell aggregation, bilateral, grade 1

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Seminiferous tubules lined by Sertoli cells only, grade 1

-Vacuolated seminiferous tubules, focal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29383 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
unilateral, grade 1

PROSTATE:

-Interstitial mononuclear cell aggregation, focal, grade 1

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number
-Round spermatids (steps 1-9) present/normal number
-Spermatocytes present/normal number
-Spermatogonia present/normal number
-Different stages of spermatogenic cycle present

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29384 SEX : MALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

PROSTATE:

-Epithelial cell atrophy, grade 2

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Degenerated/necrotic cells sloughed in lumen, grade 2

-Seminiferous tubules lined by Sertoli cells only, focal,
grade 2

-Vacuolated sertoli cells, focal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29385 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 24.11.03
DAYS ON TEST : 123
DATE OF NECROPSY : 24.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

- Sinusoidal ectasia sometimes with blood extravasation,
unilateral, grade 1
- Cyst(s), unilateral

PROSTATE:

- Epithelial cell atrophy, grade 1

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
- Round spermatids (steps 1-9) present/normal number
- Spermatocytes present/normal number
- Spermatogonia present/normal number
- Different stages of spermatogenic cycle present

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29386 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 25.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 25.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

PROSTATE:

-Epithelial cell atrophy, grade 2

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Seminiferous tubules lined by Sertoli cells only, focal,
grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29387 SEX : MALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 25.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 25.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

KIDNEYS:

01: RIGHT: MASS GREYISH/WHITISH, APPROX 4.5 CM LONG, APPROX 3.5
CM WIDE, FIRM, HOMOGENOUS, NODULAR.

02: LEFT: MASS GREYISH/WHITISH, APPROX 3 CM LONG, APPROX 2 CM
WIDE, FIRM, HOMOGENOUS, NODULAR.

03: LEFT: ENLARGED.

SPLEEN:

01: ENLARGED.

URINARY BLADDER:

01: MUCOSA: THICKENED.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Interstitial mononuclear cell aggregation, unilateral, grade 1

-Sinusoidal ectasia sometimes with blood extravasation,
unilateral, grade 1

-Cyst(s), unilateral

PROSTATE:

-Atrophy of tubulo-alveolar units, grade 2

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Seminiferous tubules lined by Sertoli cells only, focal,

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

CONT./FF. ANIMAL NO. : B29387
.....

grade 1

KIDNEYS:

-Nephroblastoma, bilateral (malignant neoplasm)

This finding corresponds to necropsy observations nos: 01,02,03.

SPLEEN:

-Lymphoid cell hyperplasia, grade 2

This finding corresponds to necropsy observation no: 01.

-Extramedullary hematopoiesis, grade 2

This finding corresponds to necropsy observation no: 01.

URINARY BLADDER:

Nothing abnormal discovered corresponding with the necropsy
observation no.01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29388 SEX : MALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 25.11.03
DAYS ON TEST : 123
DATE OF NECROPSY : 25.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
- Round spermatids (steps 1-9) present/normal number
- Spermatocytes present/normal number
- Spermatogonia present/normal number
- Different stages of spermatogenic cycle present

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29389 SEX : MALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 25.11.03
DAYS ON TEST : 123
DATE OF NECROPSY : 25.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

PROSTATE:

-Epithelial cell atrophy, grade 2

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Seminiferous tubules lined by Sertoli cells only, focal,
grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29390 SEX : MALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 25.11.03
DAYS ON TEST : 123
DATE OF NECROPSY : 25.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

LIVER:

01: ENLARGED.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 2

-Vacuolated cortical cell, bilateral, grade 2

PITUITARY GLAND:

-Developmental cyst(s), multiple

PROSTATE:

-Interstitial mononuclear cell aggregation, grade 1

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Degenerated/necrotic cells sloughed in lumen, grade 1

-Seminiferous tubules lined by Sertoli cells only, focal,
grade 1

LIVER:

-Mononuclear cell aggregation, grade 1

-Hepatocellular hypertrophy, centri-lobular, grade 2

hepatocytes show enlarged clear cytoplasm with refringent
cytoplasmic membrane at periphery

This finding corresponds to necropsy observation no: 01.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

CONT./FF. ANIMAL NO. : B29390

.....
ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29391 SEX : MALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

TESTES:

01: RIGHT: REDUCED IN SIZE, SOFT.

EPIDIDYMIDES:

01: RIGHT: REDUCED IN SIZE.

KIDNEYS:

01: IRREGULAR COLOR.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Interstitial mononuclear cell aggregation, bilateral, grade 1

PITUITARY GLAND:

Organ examined, no pathologic findings noted

PROSTATE:

-Epithelial cell atrophy, grade 2

SEMINAL VESICLES+ COAGULATING GLANDS:

Organ examined, no pathologic findings noted

TESTIS, RIGHT:

-Reduced number of tailed spermatids, grade 4

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Reduced round spermatids, grade 4

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Spermatocytes reduced in number, grade 4

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Spermatogonia Reduced, grade 4

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

CONT./FF. ANIMAL NO. : B29391
.....

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Different stages of cycle disturbed, grade 4

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Seminiferous tubules lined by Sertoli cells only, grade 4

This finding corresponds to necropsy observation no.: 01
in the TESTES.

-Vacuolated sertoli cells, grade 3

This finding corresponds to necropsy observation no.: 01
in the TESTES.

EPIDIDYMIS (RIGHT):

-Oligospermia, grade 4

This finding corresponds to necropsy observation no.: 01
in the EPIDIDYMIDES.

TESTES:

Organ not examined

For diagnosis of necropsy observation no. 01 see under:
TESTIS, RIGHT.

EPIDIDYMIDES:

Organ not examined

For diagnosis of necropsy observation no. 01 see under:
EPIDIDYMIS (RIGHT).

KIDNEYS:

-Tubular basophilia, unilateral, grade 1

-Peritubular fibrosis, unilateral, grade 1

-Acidophilic globules in cortical tubular epithelium, bilateral,
grade 4

This finding corresponds to necropsy observation no: 01.

-Interstitial mononuclear cell aggregation, unilateral, grade 1

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29392 SEX : MALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

PROSTATE:

- Epithelial cell atrophy, grade 2
- Interstitial mononuclear cell aggregation, focal, grade 1

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
- Round spermatids (steps 1-9) present/normal number
- Spermatocytes present/normal number
- Spermatogonia present/normal number
- Different stages of spermatogenic cycle present
- Seminiferous tubules lined by Sertoli cells only, focal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29393 SEX : MALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
unilateral, grade 1

PITUITARY GLAND:

-Vacuolated cells, grade 1

PROSTATE:

-Subacute prostatitis, grade 2

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Degenerated/necrotic cells sloughed in lumen, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29394 SEX : MALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
- Round spermatids (steps 1-9) present/normal number
- Spermatocytes present/normal number
- Spermatogonia present/normal number
- Different stages of spermatogenic cycle present
- Seminiferous tubules lined by Sertoli cells only, focal,
grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29395 SEX : MALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

PITUITARY GLAND:

-Vacuolated cells, grade 1

PROSTATE:

-Epithelial cell atrophy, grade 3

-Interstitial mononuclear cell aggregation, grade 1

TESTIS, RIGHT:

-Reduced number of tailed spermatids, occasional, grade 1
two tubules

-Reduced round spermatids, one tubule, grade 1

-Spermatocytes reduced in number, one tubule, grade 1

-Spermatogonia Reduced, one tubule, grade 1

-Different stages of spermatogenic cycle present

-Vacuolated seminiferous tubules, focal, grade 1

-Multinucleated Giant Cells, focal, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29396 SEX : MALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
unilateral, grade 1

PITUITARY GLAND:

-Vacuolated cells, grade 1

PROSTATE:

-Subacute prostatitis, grade 3

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29397 SEX : MALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 124
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Vacuolated cortical cell, bilateral, grade 2

PITUITARY GLAND:

-Vacuolated cells, grade 1

PROSTATE:

-Subacute prostatitis, grade 1

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29398 SEX : MALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 123
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

TESTES:

01: LEFT: TRANSLUCENT ASPECT.

EPIDIDYMIDES:

01: LEFT: REDUCED IN SIZE, TRANSLUCENT ASPECT.

KIDNEYS:

01: RIGHT: DILATED PELVIS.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 2

PITUITARY GLAND:

Organ examined, no pathologic findings noted

PROSTATE:

-Interstitial mononuclear cell aggregation, grade 1

SEMINAL VESICLES+ COAGULATING GLANDS:

Organ examined, no pathologic findings noted

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Degenerated/necrotic cells sloughed in lumen, grade 2

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

CONT./FF. ANIMAL NO. : B29398
.....

EPIDIDYMIS (RIGHT):

Organ examined, no pathologic findings noted

TESTES:

Organ not examined

Tissue with necropsy observation no.01 not submitted for
microscopic examination.

EPIDIDYMIDES:

Organ not examined

Tissue with necropsy observation no.01 not submitted for
microscopic examination.

KIDNEYS:

-Dilated pelvis, unilateral, grade 2

This finding corresponds to necropsy observation no: 01.

-Acidophilic globules in cortical tubular epithelium, bilateral,
grade 2

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29399 SEX : MALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 123
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

LIVER:

01: ENLARGED, ACCENTUATED LOBULAR PATTERN.

KIDNEYS:

01: GREY/GREEN COLOR.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

PITUITARY GLAND:

-Vacuolated cells, grade 2

PROSTATE:

-Epithelial cell atrophy, grade 2

-Interstitial mononuclear cell aggregation, grade 1

-Granulocyte infiltration, multifocal, grade 1

TESTIS, RIGHT:

-Tailed spermatids (steps 10-19) present/normal number

-Round spermatids (steps 1-9) present/normal number

-Spermatocytes present/normal number

-Spermatogonia present/normal number

-Different stages of spermatogenic cycle present

-Seminiferous tubules lined by Sertoli cells only, focal,
grade 1

LIVER:

-Altered cell foci acidophilic, one, grade 1

-Altered cell foci clear, multiple, grade 1

-Mononuclear cell aggregation, grade 2

sometimes with single cell necrosis

-Hepatocellular hypertrophy, centri-lobular, grade 3

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

CONT./FF. ANIMAL NO. : B29399
.....

characterized by enlarged clear cytoplasm and/or refringent
cytoplasmic membrane

This finding corresponds to necropsy observation no: 01.

KIDNEYS:

- Tubular basophilia, bilateral, grade 1
- Peritubular fibrosis, bilateral, grade 1
- Acidophilic globules in cortical tubular epithelium, bilateral,
grade 3

This finding corresponds to necropsy observation no: 01.

- Interstitial mononuclear cell aggregation, unilateral, grade 1

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29400 SEX : MALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 26.11.03
DAYS ON TEST : 123
DATE OF NECROPSY : 26.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

- Interstitial mononuclear cell aggregation, bilateral, grade 1
- Sinusoidal ectasia sometimes with blood extravasation, unilateral, grade 1
- Vacuolated cortical cell, bilateral, grade 2
- Altered cell foci, unilateral, grade 1
- Cystic degeneration, focal, unilateral, grade 1

PROSTATE:

- Epithelial cell atrophy, grade 3
- Interstitial mononuclear cell aggregation, grade 1

TESTIS, RIGHT:

- Tailed spermatids (steps 10-19) present/normal number
- Round spermatids (steps 1-9) present/normal number
- Spermatocytes present/normal number
- Spermatogonia present/normal number
- Different stages of spermatogenic cycle present
- Degenerated/necrotic cells sloughed in lumen, grade 2

EPIDIDYMIS (RIGHT):

- Interstitial mononuclear cell aggregation, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29776 SEX : FEMALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 18.11.03
DAYS ON TEST : 119
DATE OF NECROPSY : 18.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

UTERUS:

01: BOTH HORNS: SEROUS CONTENTS.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

- Accessory adrenal cortex, unilateral
- Cystic degeneration, unilateral, grade 1

OVARIES:

- Proestrus, bilateral

UTERUS:

- Proestrus, with morphology of previous pseudo-pregnancy

This finding corresponds to necropsy observation no: 01.

VAGINA:

- Proestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29777 SEX : FEMALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 07.09.03
DAYS ON TEST : 47
DATE OF NECROPSY : 07.09.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : FOUND DEAD
.....

* NECROPSY FINDINGS

GENERAL OBSERVATION:

01: DIED AFTER TREATMENT.
NO OTHER NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

NO EXAMINATION REQUIRED.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29778 SEX : FEMALE
FIRST DAY ON TEST : 23.07.03
LAST DAY ON TEST : 27.10.03
DAYS ON TEST : 97
DATE OF NECROPSY : 27.10.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 2

OVARIES:

-Estrus, bilateral

UTERUS:

poor quality

VAGINA:

-Estrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29779 SEX : FEMALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 14.11.03
DAYS ON TEST : 114
DATE OF NECROPSY : 14.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

- Interstitial mononuclear cell aggregation, unilateral, grade 1
- Sinusoidal ectasia sometimes with blood extravasation,
unilateral, grade 1

PITUITARY GLAND:

- Developmental cyst(s)

OVARIES:

- Estrus, bilateral

OVIDUCTS:

Organ examined, no pathologic findings noted

UTERUS:

- Estrus

VAGINA:

- Estrus
-

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29780 SEX : FEMALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 17.11.03
DAYS ON TEST : 117
DATE OF NECROPSY : 17.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

PITUITARY GLAND:

-Developmental cyst(s)

OVARIES:

-Proestrus, bilateral

OVIDUCTS:

Organ examined, no pathologic findings noted

UTERUS:

-Proestrus

-Dilated lumen, 1/2 horns, grade 1

VAGINA:

-Proestrus, residual mucification/previous pseudo-pregnancy

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29781 SEX : FEMALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 17.11.03
DAYS ON TEST : 117
DATE OF NECROPSY : 17.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

- Accessory adrenal cortex, unilateral
- Interstitial mononuclear cell aggregation, focal, unilateral,
grade 1

OVARIES:

- Proestrus, bilateral

OVIDUCTS:

Only one of paired organs examined/present

UTERUS:

- Proestrus
- Yellowish pigment laden macrophages, 1/2 horns, grade 2

VAGINA:

- Proestrus, residual mucification/previous pseudo-pregnancy

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29782 SEX : FEMALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 14.11.03
DAYS ON TEST : 114
DATE OF NECROPSY : 14.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Lipomatosis, unilateral, grade 1

OVARIES:

-Diestrus, bilateral

UTERUS:

-Diestrus

-Yellowish pigment laden macrophages, 1/2 horns, grade 2

VAGINA:

-Diestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29783 SEX : FEMALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 17.11.03
DAYS ON TEST : 117
DATE OF NECROPSY : 17.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Interstitial mononuclear cell aggregation, focal, unilateral,
grade 1

OVARIES:

-Proestrus, bilateral

UTERUS:

-Proestrus

-Yellowish pigment laden macrophages, 1/2 horns, grade 1

VAGINA:

-Proestrus, residual mucification/previous pseudo-pregnancy

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29784 SEX : FEMALE
FIRST DAY ON TEST : 24.07.03
LAST DAY ON TEST : 14.11.03
DAYS ON TEST : 114
DATE OF NECROPSY : 14.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

PITUITARY GLAND:

-Cyst(s), pars intermedia, grade 1

OVARIES:

-Estrus, bilateral

UTERUS:

-Estrus

-Yellowish pigment laden macrophages, 1/2 horns, grade 1

VAGINA:

-Estrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29785 SEX : FEMALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 14.11.03
DAYS ON TEST : 113
DATE OF NECROPSY : 14.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

PALPABLE MASSES:

01: MASS WHITISH, APPROX 1.5 CM LONG, APPROX 1.5 CM WIDE, FIRM,
HOMOGENEOUS.

NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

OVARIES:

-Diestrus, bilateral

UTERUS:

-Diestrus

-Yellowish pigment laden macrophages, both horns, grade 1
with perivascular hyalinosis

VAGINA:

-Diestrus

PALPABLE MASSES:

-Mammary Fibroadenoma (benign neoplasm)

This finding corresponds to necropsy observation no: 01.

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29786 SEX : FEMALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 22.10.03
DAYS ON TEST : 90
DATE OF NECROPSY : 22.10.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

OVARIES:

-Estrus, bilateral

UTERUS:

poor quality

VAGINA:

-Estrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29787 SEX : FEMALE
FIRST DAY ON TEST : 25.07.03
LAST DAY ON TEST : 22.10.03
DAYS ON TEST : 90
DATE OF NECROPSY : 22.10.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

- Interstitial mononuclear cell aggregation, bilateral, grade 1
- Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

OVARIES:

- Pregnancy corpora lutea, bilateral

UTERUS:

- Morphology of pregnancy

VAGINA:

- Mucification vaginal epithelium, grade 3

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29788 SEX : FEMALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 14.11.03
DAYS ON TEST : 112
DATE OF NECROPSY : 14.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

OVARIES:

-Diestrus, bilateral

UTERUS:

-Diestrus

-Yellowish pigment laden macrophages, 1/2 horns, grade 2
1/2 horns missing

VAGINA:

-Diestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29789 SEX : FEMALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 17.11.03
DAYS ON TEST : 115
DATE OF NECROPSY : 17.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

GENERAL OBSERVATION:

01: CLINICAL OBSERVATIONS NOT SEEN AT NECROPSY, NECROSED TAIL.
NO OTHER NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
unilateral, grade 2

UTERUS:

-Infolding endometrial epithelium, both horns, grade 3

VAGINA:

-Mucification vaginal epithelium, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29790 SEX : FEMALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 17.11.03
DAYS ON TEST : 115
DATE OF NECROPSY : 17.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
unilateral, grade 1

OVIDUCTS:

Only one of paired organs examined/present

UTERUS:

-Yellowish pigment laden macrophages, both horns, grade 2

VAGINA:

-Mucification vaginal epithelium, grade 2

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29791 SEX : FEMALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 13.11.03
DAYS ON TEST : 111
DATE OF NECROPSY : 13.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
unilateral, grade 1

OVARIES:

-Estrus, bilateral

UTERUS:

-Estrus

VAGINA:

-Estrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29792 SEX : FEMALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 17.11.03
DAYS ON TEST : 115
DATE OF NECROPSY : 17.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

- Cortical cell hypertrophy, focal, unilateral, grade 2
- Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 2

OVARIES:

- Diestrus, bilateral

OVIDUCTS:

Only one of paired organs examined/present

UTERUS:

- Diestrus
- Yellowish pigment laden macrophages, 1/2 horns, grade 3
sometimes with hyalinosis

VAGINA:

- Diestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29793 SEX : FEMALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 13.11.03
DAYS ON TEST : 111
DATE OF NECROPSY : 13.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

- Interstitial mononuclear cell aggregation, focal, unilateral, grade 1
- Sinusoidal ectasia sometimes with blood extravasation, unilateral, grade 2

OVARIES:

- Diestrus, bilateral

OVIDUCTS:

Only one of paired organs examined/present

UTERUS:

- Diestrus
- Yellowish pigment laden macrophages, 1/2 horns, grade 2

VAGINA:

- Diestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29794 SEX : FEMALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 13.11.03
DAYS ON TEST : 111
DATE OF NECROPSY : 13.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

OVARIES:

-Diestrus, bilateral

UTERUS:

-Diestrus

VAGINA:

-Diestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29795 SEX : FEMALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 14.11.03
DAYS ON TEST : 112
DATE OF NECROPSY : 14.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

- Accessory adrenal cortex, unilateral
- Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

OVARIES:

- Diestrus, bilateral

UTERUS:

- Diestrus
- Yellowish pigment laden macrophages, 1/2 horns, grade 2

VAGINA:

- Diestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29796 SEX : FEMALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 12.11.03
DAYS ON TEST : 110
DATE OF NECROPSY : 12.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
unilateral, grade 1

OVARIES:

-Diestrus, bilateral

OVIDUCTS:

Only one of paired organs examined/present

UTERUS:

-Diestrus

-Yellowish pigment laden macrophages, 1/2 horns, grade 3

VAGINA:

-Diestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29797 SEX : FEMALE
FIRST DAY ON TEST : 26.07.03
LAST DAY ON TEST : 13.11.03
DAYS ON TEST : 111
DATE OF NECROPSY : 13.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

OVARIES:

-Metestrus, bilateral

UTERUS:

-Metestrus

-Yellowish pigment laden macrophages, 1/2 horns, grade 2
with hyalinosis

VAGINA:

-Metestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29798 SEX : FEMALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 22.10.03
DAYS ON TEST : 88
DATE OF NECROPSY : 22.10.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

OVARIES:

-Pregnancy corpora lutea, bilateral

UTERUS:

-Morphology of pregnancy

VAGINA:

-Mucification vaginal epithelium, grade 4

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29799 SEX : FEMALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 27.10.03
DAYS ON TEST : 93
DATE OF NECROPSY : 27.10.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : SACRIFICED MORIBUND
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

OVARIES:

-Diestrus, bilateral

OVIDUCTS:

Only one of paired organs examined/present

UTERUS:

-Diestrus

-Yellowish pigment laden macrophages, 1/2 horns, grade 2
with hyalinosis around blood vessels

VAGINA:

-Diestrus

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

CIT/Study No. 24859 RSR/ETHYL TERTIARY BUTYL ETHER (ETBE)/
TOTAL France S.A.

TEXT OF GROSS AND MICROSCOPIC FINDINGS

DOSE GROUP : 4, 1000mg/kg/d.F1

* ANIMAL NUMBER : B29800 SEX : FEMALE
FIRST DAY ON TEST : 27.07.03
LAST DAY ON TEST : 17.11.03
DAYS ON TEST : 114
DATE OF NECROPSY : 17.11.03
DEFINED SACR.GROUP : TERMINAL SACRIFICE GROUP
STATUS AT NECROPSY : TERMINAL SACRIFICE GROUP
.....

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

ADRENAL GLANDS:

-Sinusoidal ectasia sometimes with blood extravasation,
bilateral, grade 1

OVARIES:

-Proestrus, early, bilateral

OVIDUCTS:

Only one of paired organs examined/present

UTERUS:

-Proestrus, early

VAGINA:

-Proestrus, early

ALL OTHER PROTOCOL TISSUES WITHOUT PATHOLOGIC FINDINGS.

68. F1 generation - number of primordial and growing follicles counted for each female,
for both ovaries

Individual data - F1 parents
Number of primordial and growing follicles counted
for each female, for both ovaries

Dose: 0 mg/kg/day

Sex: female

| Animal No. | Number of primordial follicles | Number of growing follicles |
|--------------|--------------------------------|-----------------------------|
| B29701 | 7 | 3 |
| B29702 | 9 | 5 |
| B29703 | 4 | 5 |
| B29704 | 19 | 2 |
| B29705 | 19 | 1 |
| B29706 | 41 | 1 |
| B29707 | 28 | 2 |
| B29708 | 18 | 2 |
| B29709 | 14 | 3 |
| B29710 | 14 | 4 |
| B29711 | 34 | 4 |
| B29712 | 20 | 5 |
| B29713 | 4 | 2 |
| B29714 | 39 | 6 |
| B29715 | 15 | 3 |
| B29716 | 35 | 3 |
| B29717 | 20 | 1 |
| B29718 | 27 | 12 |
| B29719 | 18 | 3 |
| B29720 | 15 | 3 |
| B29721 | 13 | 2 |
| B29722 | 11 | 1 |
| B29723 | 40 | 8 |
| B29724 | 19 | 2 |
| B29725 | 2 | 3 |
| Total number | 485 | 86 |
| Mean value | 19.40 | 3.44 |
| Range | 2/41 | 1/12 |

Individual data - F1 parents
Number of primordial and growing follicles counted
for each female, for both ovaries

Dose: 1000 mg/kg/day

Sex: female

| Animal No. | Number of primordial follicles | Number of growing follicles |
|--------------|--------------------------------|-----------------------------|
| B29776 | 12 | 3 |
| B29778 | 10 | 2 |
| B29779 | 10 | 2 |
| B29780 | 2 | 1 |
| B29781 | 16 | 1 |
| B29782 | 8 | 3 |
| B29783 | 18 | 6 |
| B29784 | 8 | 5 |
| B29785 | 16 | 2 |
| B29786 | 51 | 8 |
| B29787 | 10 | 1 |
| B29788 | 16 | 1 |
| B29789 | 9 | 1 |
| B29790 | 13 | 2 |
| B29791 | 18 | 1 |
| B29792 | 35 | 2 |
| B29793 | 21 | 1 |
| B29794 | 14 | 1 |
| B29795 | 21 | 3 |
| B29796 | 8 | 0 |
| B29797 | 10 | 0 |
| B29798 | 21 | 5 |
| B29799 | 21 | 0 |
| B29800 | 15 | 1 |
| Total number | 383 | 52 |
| Mean value | 15.32 | 2.08 |
| Range | 2/51 | 0/8 |

69. Maternal origin of F2 pups/study number of F2 pups after weaning

MATERNAL ORIGIN OF F2 PUPS
STUDY NUMBER OF F2 PUPS AFTER WEANING

Dose-level: 0 mg/kg/day (Group 1)

| F1 female number | F2 male | | F2 female | |
|---------------------|---------|-----------|-----------|-----------|
| | pup No. | study No. | pup No. | study No. |
| B29704 | 1 | B29401 | 6 | B29801 |
| | 2 | B29402 | 7 | B29802 |
| B29718 | 1 | B29403 | 10 | B29803 |
| | 2 | B29404 | 12 | B29804 |
| B29709 | 1 | B29405 | 7 | B29805 |
| | 2 | B29406 | | |
| B29710 | 1 | B29407 | 11 | B29806 |
| | | | 12 | B29807 |
| B29711 | 1 | B29408 | 11 | B29808 |
| | | | 12 | B29809 |
| B29708 | 2 | B29409 | 10 | B29810 |
| B29719 | 1 | B29410 | 8 | B29811 |
| B29721 | 1 | B29411 | 7 | B29812 |
| B29722 | 1 | B29412 | 12 | B29813 |
| B29723 | 1 | B29413 | 8 | B29814 |
| B29701 | 1 | B29414 | 8 | B29815 |
| B29702 | 1 | B29415 | 7 | B29816 |
| B29705 | 1 | B29416 | 8 | B29817 |
| B29706 | 1 | B29417 | 9 | B29818 |
| B29713 | 1 | B29418 | 8 | B29819 |
| B29724 | 1 | B29420 | 6 | B29821 |
| B29725 | 1 | B29421 | 9 | B29822 |
| | 2 | B29419 | 10 | B29820 |
| B29715 | 1 | B29422 | 8 | B29823 |
| | 2 | B29423 | 9 | B29824 |
| B29717 | 1 | B29424 | 7 | B29825 |
| | 2 | B29425 | | |

MATERNAL ORIGIN OF F2 PUPS
STUDY NUMBER OF F2 PUPS AFTER WEANING

Dose-level: 250 mg/kg/day (Group 2)

| F1 female number | F2 male | | F2 female | |
|---------------------|---------|-----------|-----------|-----------|
| | pup No. | study No. | pup No. | study No. |
| B29729 | 1 | B29426 | 8 | B29826 |
| | 2 | B29427 | 9 | B29827 |
| B29731 | 1 | B29428 | 8 | B29828 |
| B29736 | 1 | B29429 | 10 | B29829 |
| B29742 | 1 | B29430 | 5 | B29830 |
| B29743 | 1 | B29431 | 7 | B29831 |
| B29748 | 1 | B29432 | 8 | B29832 |
| B29749 | 1 | B29433 | 6 | B29833 |
| B29728 | 1 | B29434 | 9 | B29834 |
| | 2 | B29435 | 10 | B29835 |
| B29733 | 1 | B29436 | 6 | B29836 |
| | 2 | B29437 | 7 | B29837 |
| B29740 | 2 | B29438 | 7 | B29838 |
| | | | 8 | B29839 |
| B29726 | 1 | B29439 | 8 | B29840 |
| | 2 | B29440 | 9 | B29841 |
| B29750 | 1 | B29441 | 11 | B29842 |
| | 2 | B29442 | 12 | B29843 |
| B29735 | 1 | B29443 | 7 | B29844 |
| | 2 | B29444 | 8 | B29845 |
| B29741 | 1 | B29445 | 9 | B29846 |
| | 2 | B29446 | 10 | B29847 |
| B29744 | 1 | B29447 | 8 | B29848 |
| | 2 | B29448 | | |
| B29745 | 1 | B29449 | 8 | B29849 |
| B29747 | 1 | B29450 | 9 | B29850 |

MATERNAL ORIGIN OF F2 PUPS
STUDY NUMBER OF F2 PUPS AFTER WEANING

Dose-level: 500 mg/kg/day (Group 3)

| F1 female number | F2 male | | F2 female | |
|---------------------|---------|-----------|-----------|-----------|
| | pup No. | study No. | pup No. | study No. |
| B29766 | 1 | B29451 | 10 | B29851 |
| | 2 | B29452 | 11 | B29852 |
| B29755 | 1 | B29453 | 6 | B29853 |
| B29760 | 1 | B29454 | 13 | B29854 |
| B29765 | 1 | B29455 | 5 | B29855 |
| B29769 | 1 | B29456 | 6 | B29856 |
| B29772 | 1 | B29457 | 8 | B29857 |
| B29775 | 1 | B29458 | 7 | B29858 |
| B29752 | 1 | B29459 | 6 | B29859 |
| | 2 | B29460 | 7 | B29860 |
| B29753 | 1 | B29461 | 6 | B29861 |
| | 2 | B29462 | 7 | B29862 |
| B29768 | 1 | B29463 | 5 | B29863 |
| B29770 | 1 | B29464 | 10 | B29864 |
| B29774 | 1 | B29465 | 4 | B29865 |
| B29751 | 1 | B29466 | 7 | B29866 |
| B29756 | 1 | B29467 | 9 | B29867 |
| B29757 | 1 | B29468 | 9 | B29868 |
| B29758 | 1 | B29469 | 9 | B29869 |
| B29759 | 1 | B29470 | 8 | B29870 |
| B29763 | 1 | B29471 | 11 | B29871 |
| B29764 | 1 | B29472 | 8 | B29872 |
| B29771 | 1 | B29473 | 8 | B29873 |
| B29754 | 1 | B29474 | 9 | B29874 |
| | 2 | B29475 | 10 | B29875 |

MATERNAL ORIGIN OF F2 PUPS
STUDY NUMBER OF F2 PUPS AFTER WEANING

Dose-level: 1000 mg/kg/day (Group 4)

| F1 female number | F2 male | | F2 female | |
|---------------------|---------|-----------|-----------|-----------|
| | pup No. | study No. | pup No. | study No. |
| B29796 | 1 | B29476 | 9 | B29876 |
| | 2 | B29477 | 10 | B29877 |
| B29791 | 1 | B29478 | 7 | B29878 |
| | 2 | B29479 | 8 | B29879 |
| B29793 | 1 | B29480 | 6 | B29880 |
| | 2 | B29481 | 7 | B29881 |
| B29794 | 1 | B29482 | 9 | B29882 |
| | 2 | B29483 | 10 | B29883 |
| B29797 | 1 | B29484 | 6 | B29884 |
| | 2 | B29485 | 7 | B29885 |
| B29779 | 1 | B29486 | 9 | B29886 |
| B29782 | 1 | B29487 | 10 | B29887 |
| B29784 | 1 | B29488 | 13 | B29888 |
| B29785 | 1 | B29489 | 10 | B29889 |
| B29788 | 1 | B29490 | 9 | B29890 |
| B29795 | 1 | B29491 | 6 | B29891 |
| B29780 | 1 | B29492 | 9 | B29892 |
| B29781 | 1 | B29493 | 9 | B29893 |
| B29783 | 1 | B29494 | 7 | B29894 |
| B29789 | 2 | B29495 | 9 | B29895 |
| B29790 | 1 | B29496 | 8 | B29896 |
| B29497 | 1 | B29497 | 9 | B29897 |
| B29800 | 1 | B29498 | 7 | B29898 |
| B29776 | 1 | B29499 | 5 | B29899 |
| | 2 | B29500 | 6 | B29900 |

70. F2 generation - clinical history (individual findings/males)

F2 GENERATION

CLINICAL HISTORY (Individual findings/Males)

MALES Dose: 0 mg/kg/day

| ANIMAL# | OBSERVATIONS | DAYS OBSERVED | |
|---------|--|--|--------------------------------------|
| B29401 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29402 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29403 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29404 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29405 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29406 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29407 | Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTVALISM immediately post-dosing | 1 to 20, 25 to end 27 21 to 24 |
| B29408 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29409 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29410 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29411 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29412 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29413 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29414 | Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |

F2 GENERATION

CLINICAL HISTORY (Individual findings/Males)

MALES Dose: 0 mg/kg/day

| ANIMAL# | OBSERVATIONS | DAYS OBSERVED |
|---|--|-----------------------------|
| B29414 (CONTINUED) Mortality | FINAL SACRIFICE | 27 |
| B29415 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29416 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29417 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29418 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29419 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29420 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29421 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29422 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29423 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29424 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29425 Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 4, 6 to end 27 5 |

F2 GENERATION

CLINICAL HISTORY (Individual findings/Males)

MALES Dose: 250 mg/kg/day

| ANIMAL# | | OBSERVATIONS | DAYS OBSERVED |
|---------|--|--|--------------------------------------|
| B29426 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29427 | Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 14, 26 to end 27 15 to 25 |
| B29428 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29429 | Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 21, 27 27 22 to 26 |
| B29430 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29431 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29432 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29433 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29434 | Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 12, 14 to end 27 13 |
| B29435 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29436 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29437 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29438 | Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |

F2 GENERATION

CLINICAL HISTORY (Individual findings/Males)

MALES Dose: 250 mg/kg/day

| ANIMAL# | OBSERVATIONS | DAYS OBSERVED |
|---|--|------------------------------------|
| B29438 (CONTINUED) Mortality | FINAL SACRIFICE | 27 |
| B29439 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29440 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29441 Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 15, 27 27 16 to 26 |
| B29442 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29443 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29444 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29445 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29446 Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 22, 27 27 23 to 26 |
| B29447 Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 20, 27 27 21 to 26 |
| B29448 Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 5, 19 to end 27 6 to 18 |
| B29449 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29450 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to 22, 27 27 |

F2 GENERATION

CLINICAL HISTORY (Individual findings/Males)

MALES Dose: 250 mg/kg/day

| ANIMAL# | OBSERVATIONS | DAYS OBSERVED |
|--------------------|--|---------------|
| B29450 (CONTINUED) | Secretion/Excretion PTYALISM immediately post-dosing | 23 to 26 |

F2 GENERATION

CLINICAL HISTORY (Individual findings/Males)

MALES Dose: 500 mg/kg/day

| ANIMAL# | OBSERVATIONS | DAYS OBSERVED | |
|---------|--|--|-------------------------------|
| B29451 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29452 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29453 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29454 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29455 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29456 | Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 18, 27 27 19 to 26 |
| B29457 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29458 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29459 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29460 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29461 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29462 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29463 | Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 21, 27 27 22 to 26 |

F2 GENERATION

CLINICAL HISTORY (Individual findings/Males)

MALES Dose: 500 mg/kg/day

| ANIMAL# | | OBSERVATIONS | DAYS OBSERVED |
|---------|--|--|-------------------------------|
| B29464 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29465 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29466 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29467 | Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 23, 27 27 24 to 26 |
| B29468 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29469 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29470 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29471 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29472 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29473 | Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 5, 7 to end 27 6 |
| B29474 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29475 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |

F2 GENERATION

CLINICAL HISTORY (Individual findings/Males)

MALES Dose: 1000 mg/kg/day

| ANIMAL# | | OBSERVATIONS | DAYS OBSERVED |
|---------|--|--|--|
| B29476 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29477 | Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 14, 27 27 15 to 26 |
| B29478 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29479 | Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 18, 22 to end 27 19 to 21 |
| B29480 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29481 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29482 | Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 13, 27 27 14 to 26 |
| B29483 | Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 12, 14, 17 to 20, 23 to end 27 13, 15 to 16, 21 to 22 |
| B29484 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29485 | Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 22, 27 27 23 to 26 |
| B29486 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29487 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to 16, 20 to 24, 27 27 |

F2 GENERATION

CLINICAL HISTORY (Individual findings/Males)

MALES Dose: 1000 mg/kg/day

| ANIMAL# | OBSERVATIONS | DAYS OBSERVED |
|---------------------|---|----------------------------|
| B29487 (CONTINUED) | | |
| Secretion/Excretion | PTYALISM immediately post-dosing | 17 to 19, 25 to 26 |
| B29488 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to 16, 25 to end |
| Mortality | FINAL SACRIFICE | 27 |
| Secretion/Excretion | PTYALISM immediately post-dosing | 17 to 24 |
| B29489 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |
| B29490 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |
| B29491 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to 24, 27 |
| Mortality | FINAL SACRIFICE | 27 |
| Secretion/Excretion | PTYALISM immediately post-dosing | 25 to 26 |
| B29492 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |
| B29493 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to 15, 24 to end |
| Mortality | FINAL SACRIFICE | 27 |
| Secretion/Excretion | PTYALISM immediately post-dosing | 16 to 23 |
| B29494 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |
| B29495 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |
| B29496 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to 20, 27 |
| Mortality | FINAL SACRIFICE | 27 |
| Secretion/Excretion | PTYALISM immediately post-dosing | 21 to 26 |
| B29497 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to 3, 27 |
| Mortality | FINAL SACRIFICE | 27 |
| General aspect | ROUND BACK | 4 to 6 |
| | PILOERECTION | 4 to 6 |
| Secretion/Excretion | PTYALISM immediately post-dosing | 24 to 26 |
| Miscellaneous | ABNORMAL GROWTH OF TEETH (cut regulary) | 4 to 23 |
| B29498 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to 5, 7 to 11, 13 to end |

F2 GENERATION

CLINICAL HISTORY (Individual findings/Males)

MALES Dose: 1000 mg/kg/day

| ANIMAL# | OBSERVATIONS | DAYS OBSERVED |
|---------------------|-------------------------------------|--------------------|
| B29498 (CONTINUED) | | |
| Mortality | FINAL SACRIFICE | 27 |
| Secretion/Excretion | PTYALISM immediately post-dosing | 6, 12 |
| B29499 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to 10, 23 to end |
| Mortality | FINAL SACRIFICE | 27 |
| Secretion/Excretion | PTYALISM immediately post-dosing | 11 to 22 |
| B29500 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |

71. F2 generation - clinical history (individual findings/females/premating period)

F2 GENERATION

CLINICAL HISTORY (Individual findings/Females/Premating period)

FEMALES Dose: 0 mg/kg/day

| ANIMAL# | | OBSERVATIONS | DAYS OBSERVED |
|---------|---------------------|---|----------------|
| B29801 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29802 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29803 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29804 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29805 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29806 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29807 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29808 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29809 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29810 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29811 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FOUND DEAD (after treatment) | 1 to end 25 |
| B29812 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29813 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29814 | Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |

F2 GENERATION

CLINICAL HISTORY (Individual findings/Females/Premating period)

FEMALES Dose: 0 mg/kg/day

| ANIMAL# | OBSERVATIONS | DAYS OBSERVED |
|---------------------------------|--|----------------|
| B29814 (CONTINUED) Mortality | FINAL SACRIFICE | 27 |
| B29815 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29816 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29817 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29818 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29819 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29820 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29821 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29822 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29823 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29824 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29825 Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |

F2 GENERATION

CLINICAL HISTORY (Individual findings/Females/Premating period)

FEMALES Dose: 250 mg/kg/day

| ANIMAL# | | OBSERVATIONS | DAYS OBSERVED |
|---------|---------------------|--|----------------|
| B29826 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29827 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29828 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29829 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29830 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29831 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29832 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29833 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29834 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29835 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29836 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29837 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29838 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29839 | Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to 24, 27 |

F2 GENERATION

CLINICAL HISTORY (Individual findings/Females/Premating period)

FEMALES Dose: 250 mg/kg/day

| ANIMAL# | OBSERVATIONS | DAYS OBSERVED |
|---------------------|-------------------------------------|--------------------|
| B29839 (CONTINUED) | | |
| Mortality | FINAL SACRIFICE | 27 |
| Secretion/Excretion | PTYALISM immediately post-dosing | 25 to 26 |
| B29840 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |
| B29841 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |
| B29842 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |
| B29843 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to 16, 24 to end |
| Mortality | FINAL SACRIFICE | 27 |
| Secretion/Excretion | PTYALISM immediately post-dosing | 17 to 23 |
| B29844 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |
| B29845 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |
| B29846 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |
| B29847 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |
| B29848 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |
| B29849 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |
| B29850 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |

F2 GENERATION

CLINICAL HISTORY (Individual findings/Females/Premating period)

FEMALES Dose: 500 mg/kg/day

| ANIMAL# | OBSERVATIONS | DAYS OBSERVED | |
|---------|--|--|--------------------------------------|
| B29851 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29852 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29853 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29854 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29855 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29856 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29857 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29858 | Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 14, 26 to end 27 15 to 25 |
| B29859 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29860 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29861 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29862 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29863 | Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 11, 17 to end 27 12 to 16 |

F2 GENERATION

CLINICAL HISTORY (Individual findings/Females/Premating period)

FEMALES Dose: 500 mg/kg/day

| ANIMAL# | | OBSERVATIONS | DAYS OBSERVED |
|---------|--|--|--------------------------------|
| B29864 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29865 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29866 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29867 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29868 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29869 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29870 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29871 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29872 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29873 | Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 18, 20 to end 27 19 |
| B29874 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29875 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |

F2 GENERATION

CLINICAL HISTORY (Individual findings/Females/Premating period)

FEMALES Dose: 1000 mg/kg/day

| ANIMAL# | OBSERVATIONS | DAYS OBSERVED | |
|---------|--|--|--------------------------------------|
| B29876 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29877 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29878 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29879 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29880 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29881 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29882 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29883 | Normal Mortality | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE | 1 to end 27 |
| B29884 | Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 25, 27 27 26 |
| B29885 | Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 20, 26 to end 27 21 to 25 |
| B29886 | Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 24, 27 27 25 to 26 |
| B29887 | Normal Mortality Secretion/Excretion | NO REMARKABLE CLINICAL OBSERVATIONS FINAL SACRIFICE PTYALISM immediately post-dosing | 1 to 24, 27 27 25 to 26 |
| B29888 | Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to 17, 19 to end |

F2 GENERATION

CLINICAL HISTORY (Individual findings/Females/Premating period)

FEMALES Dose: 1000 mg/kg/day

| ANIMAL# | OBSERVATIONS | DAYS OBSERVED |
|---------------------|-------------------------------------|----------------------|
| B29888 (CONTINUED) | | |
| Mortality | FINAL SACRIFICE | 27 |
| Secretion/Excretion | PTYALISM immediately post-dosing | 18 |
| B29889 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |
| B29890 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |
| B29891 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |
| B29892 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to 16, 18 to end |
| Mortality | FINAL SACRIFICE | 27 |
| Secretion/Excretion | PTYALISM immediately post-dosing | 17 |
| B29893 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to 9, 12 to 23, 27 |
| Mortality | FINAL SACRIFICE | 27 |
| Secretion/Excretion | PTYALISM immediately post-dosing | 10 to 11, 24 to 26 |
| B29894 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |
| B29895 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to 11, 13 to end |
| Mortality | FINAL SACRIFICE | 27 |
| Secretion/Excretion | PTYALISM immediately post-dosing | 12 |
| B29896 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |
| B29897 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to 23, 27 |
| Mortality | FINAL SACRIFICE | 27 |
| Secretion/Excretion | PTYALISM immediately post-dosing | 24 to 26 |
| B29898 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to 23, 27 |
| Mortality | FINAL SACRIFICE | 27 |
| Secretion/Excretion | PTYALISM immediately post-dosing | 24 to 26 |
| B29899 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to end |
| Mortality | FINAL SACRIFICE | 27 |
| B29900 | | |
| Normal | NO REMARKABLE CLINICAL OBSERVATIONS | 1 to 22, 26 to end |

F2 GENERATION

CLINICAL HISTORY (Individual findings/Females/Premating period)

FEMALES Dose: 1000 mg/kg/day

| ANIMAL# | OBSERVATIONS | DAYS OBSERVED |
|---------------------|----------------------------------|---------------|
| B29900 (CONTINUED) | | |
| Mortality | FINAL SACRIFICE | 27 |
| Secretion/Excretion | PTYALISM immediately post-dosing | 23 to 26 |

72. F2 generation - body weights (individual values/grams/males)

F2 GENERATION

BODY WEIGHTS (Individual values/Grams/Males)

MALES Dose: 0 mg/kg/day

| Animal No. | Day of STUDY | | | |
|------------|--------------|-----|-----|-----|
| | 1 | 8 | 15 | 22 |
| B29401 | 52 | 92 | 149 | 217 |
| B29402 | 55 | 96 | 158 | 227 |
| B29403 | 54 | 86 | 133 | 181 |
| B29404 | 51 | 85 | 134 | 196 |
| B29405 | 54 | 89 | 136 | 194 |
| B29406 | 56 | 95 | 156 | 221 |
| B29407 | 53 | 92 | 149 | 216 |
| B29408 | 45 | 77 | 135 | 202 |
| B29409 | 45 | 83 | 140 | 209 |
| B29410 | 59 | 101 | 170 | 241 |
| B29411 | 51 | 84 | 138 | 195 |
| B29412 | 63 | 99 | 153 | 207 |
| B29413 | 52 | 89 | 137 | 188 |
| B29414 | 56 | 95 | 150 | 205 |
| B29415 | 59 | 105 | 170 | 246 |
| B29416 | 41 | 76 | 130 | 193 |
| B29417 | 56 | 95 | 151 | 217 |
| B29418 | 55 | 96 | 147 | 212 |
| B29419 | 55 | 95 | 159 | 220 |
| B29420 | 64 | 104 | 161 | 223 |
| B29421 | 55 | 93 | 155 | 220 |
| B29422 | 59 | 98 | 160 | 215 |
| B29423 | 57 | 97 | 154 | 215 |
| B29424 | 53 | 94 | 148 | 209 |
| B29425 | 46 | 88 | 142 | 207 |
| MEAN | 54 | 92 | 148 | 211 |
| S.D. | 5 | 7 | 11 | 15 |
| N | 25 | 25 | 25 | 25 |

F2 GENERATION

BODY WEIGHTS (Individual values/Grams/Males)

MALES Dose: 250 mg/kg/day

| Animal No. | Day of STUDY | | | |
|------------|--------------|-----|-----|-----|
| | 1 | 8 | 15 | 22 |
| B29426 | 53 | 86 | 138 | 186 |
| B29427 | 54 | 90 | 146 | 209 |
| B29428 | 57 | 97 | 156 | 228 |
| B29429 | 68 | 115 | 183 | 259 |
| B29430 | 60 | 96 | 153 | 214 |
| B29431 | 57 | 97 | 152 | 216 |
| B29432 | 50 | 86 | 146 | 208 |
| B29433 | 63 | 104 | 160 | 232 |
| B29434 | 54 | 87 | 148 | 211 |
| B29435 | 54 | 88 | 145 | 208 |
| B29436 | 56 | 97 | 147 | 212 |
| B29437 | 54 | 93 | 151 | 216 |
| B29438 | 50 | 85 | 131 | 186 |
| B29439 | 55 | 93 | 149 | 222 |
| B29440 | 51 | 82 | 134 | 197 |
| B29441 | 58 | 95 | 153 | 207 |
| B29442 | 60 | 95 | 146 | 204 |
| B29443 | 61 | 94 | 147 | 203 |
| B29444 | 65 | 104 | 161 | 220 |
| B29445 | 53 | 91 | 151 | 217 |
| B29446 | 55 | 94 | 156 | 222 |
| B29447 | 60 | 101 | 163 | 225 |
| B29448 | 58 | 102 | 167 | 234 |
| B29449 | 58 | 94 | 159 | 225 |
| B29450 | 59 | 101 | 167 | 235 |
| MEAN | 57 | 95 | 152 | 216 |
| S.D. | 5 | 7 | 11 | 16 |
| N | 25 | 25 | 25 | 25 |

F2 GENERATION

BODY WEIGHTS (Individual values/Grams/Males)

MALES Dose: 500 mg/kg/day

| Animal No. | Day of STUDY | | | |
|------------|--------------|-----|-----|-----|
| | 1 | 8 | 15 | 22 |
| B29451 | 40 | 68 | 104 | 157 |
| B29452 | 54 | 84 | 136 | 209 |
| B29453 | 45 | 80 | 128 | 187 |
| B29454 | 62 | 105 | 168 | 239 |
| B29455 | 49 | 92 | 153 | 217 |
| B29456 | 52 | 85 | 135 | 198 |
| B29457 | 53 | 89 | 138 | 190 |
| B29458 | 49 | 84 | 132 | 188 |
| B29459 | 55 | 96 | 152 | 220 |
| B29460 | 53 | 93 | 152 | 224 |
| B29461 | 64 | 110 | 176 | 241 |
| B29462 | 45 | 83 | 142 | 209 |
| B29463 | 50 | 87 | 142 | 204 |
| B29464 | 45 | 83 | 132 | 186 |
| B29465 | 52 | 89 | 140 | 191 |
| B29466 | 56 | 97 | 141 | 172 |
| B29467 | 49 | 83 | 138 | 203 |
| B29468 | 63 | 98 | 127 | 147 |
| B29469 | 66 | 115 | 174 | 238 |
| B29470 | 53 | 89 | 139 | 194 |
| B29471 | 64 | 105 | 151 | 190 |
| B29472 | 62 | 98 | 153 | 219 |
| B29473 | 56 | 91 | 131 | 197 |
| B29474 | 55 | 98 | 131 | 184 |
| B29475 | 58 | 101 | 162 | 225 |
| MEAN | 54 | 92 | 143 | 201 |
| S.D. | 7 | 10 | 16 | 24 |
| N | 25 | 25 | 25 | 25 |

F2 GENERATION

BODY WEIGHTS (Individual values/Grams/Males)

MALES Dose: 1000 mg/kg/day

| Animal No. | Day of STUDY | | | |
|------------|--------------|-----|-----|-----|
| | 1 | 8 | 15 | 22 |
| B29476 | 61 | 99 | 157 | 218 |
| B29477 | 60 | 107 | 166 | 242 |
| B29478 | 55 | 98 | 154 | 211 |
| B29479 | 65 | 112 | 174 | 236 |
| B29480 | 55 | 97 | 163 | 230 |
| B29481 | 55 | 90 | 146 | 205 |
| B29482 | 52 | 88 | 143 | 196 |
| B29483 | 50 | 86 | 136 | 182 |
| B29484 | 54 | 91 | 146 | 208 |
| B29485 | 55 | 96 | 147 | 214 |
| B29486 | 53 | 93 | 151 | 207 |
| B29487 | 47 | 75 | 110 | 154 |
| B29488 | 55 | 96 | 153 | 221 |
| B29489 | 63 | 104 | 169 | 243 |
| B29490 | 56 | 95 | 162 | 230 |
| B29491 | 56 | 95 | 152 | 216 |
| B29492 | 58 | 99 | 160 | 225 |
| B29493 | 53 | 87 | 142 | 205 |
| B29494 | 51 | 81 | 132 | 193 |
| B29495 | 58 | 96 | 163 | 234 |
| B29496 | 55 | 91 | 142 | 199 |
| B29497 | 40 | 50 | 93 | 147 |
| B29498 | 53 | 81 | 136 | 196 |
| B29499 | 58 | 99 | 164 | 228 |
| B29500 | 49 | 82 | 128 | 171 |
| MEAN | 55 | 91 | 148 | 208 |
| S.D. | 5 | 12 | 19 | 25 |
| N | 25 | 25 | 25 | 25 |

73. F2 generation - body weight change (individual values/grams/males)

F2 GENERATION

BODY WEIGHT CHANGE (Individual values/Grams/Males)

MALES Dose: 0 mg/kg/day

| ANIMAL# | Day OF STUDY | | |
|---------|--------------|------|-------|
| | 1-8 | 8-15 | 15-22 |
| B29401 | 40 | 57 | 68 |
| B29402 | 40 | 63 | 69 |
| B29403 | 32 | 46 | 49 |
| B29404 | 33 | 50 | 62 |
| B29405 | 34 | 47 | 58 |
| B29406 | 40 | 60 | 65 |
| B29407 | 40 | 57 | 66 |
| B29408 | 32 | 58 | 68 |
| B29409 | 38 | 57 | 68 |
| B29410 | 42 | 69 | 71 |
| B29411 | 33 | 53 | 57 |
| B29412 | 36 | 54 | 54 |
| B29413 | 37 | 48 | 52 |
| B29414 | 38 | 56 | 55 |
| B29415 | 46 | 65 | 76 |
| B29416 | 35 | 54 | 64 |
| B29417 | 39 | 56 | 66 |
| B29418 | 41 | 51 | 65 |
| B29419 | 40 | 64 | 62 |
| B29420 | 40 | 57 | 62 |
| B29421 | 39 | 61 | 65 |
| B29422 | 40 | 61 | 55 |
| B29423 | 40 | 57 | 61 |
| B29424 | 41 | 54 | 61 |
| B29425 | 42 | 54 | 65 |
| MEAN | 38 | 56 | 62 |
| S.D. | 3 | 6 | 6 |
| N | 25 | 25 | 25 |

F2 GENERATION

BODY WEIGHT CHANGE (Individual values/Grams/Males)

MALES Dose: 250 mg/kg/day

| ANIMAL# | Day OF STUDY | | |
|---------|--------------|------|-------|
| | 1-8 | 8-15 | 15-22 |
| B29426 | 33 | 52 | 48 |
| B29427 | 36 | 56 | 64 |
| B29428 | 41 | 58 | 73 |
| B29429 | 47 | 69 | 75 |
| B29430 | 36 | 57 | 61 |
| B29431 | 40 | 56 | 64 |
| B29432 | 37 | 60 | 62 |
| B29433 | 41 | 56 | 72 |
| B29434 | 34 | 61 | 63 |
| B29435 | 34 | 57 | 63 |
| B29436 | 41 | 51 | 65 |
| B29437 | 39 | 59 | 64 |
| B29438 | 35 | 46 | 56 |
| B29439 | 38 | 56 | 73 |
| B29440 | 32 | 51 | 64 |
| B29441 | 37 | 59 | 53 |
| B29442 | 35 | 51 | 58 |
| B29443 | 33 | 53 | 56 |
| B29444 | 39 | 57 | 60 |
| B29445 | 37 | 60 | 66 |
| B29446 | 38 | 63 | 66 |
| B29447 | 41 | 62 | 62 |
| B29448 | 44 | 65 | 68 |
| B29449 | 36 | 65 | 66 |
| B29450 | 42 | 66 | 67 |
| MEAN | 38 | 58 | 64 |
| S.D. | 4 | 5 | 6 |
| N | 25 | 25 | 25 |

F2 GENERATION

BODY WEIGHT CHANGE (Individual values/Grams/Males)

MALES Dose: 500 mg/kg/day

| ANIMAL# | Day OF STUDY | | |
|---------|--------------|------|-------|
| | 1-8 | 8-15 | 15-22 |
| B29451 | 28 | 36 | 53 |
| B29452 | 30 | 51 | 73 |
| B29453 | 35 | 47 | 59 |
| B29454 | 43 | 63 | 71 |
| B29455 | 43 | 61 | 64 |
| B29456 | 33 | 50 | 62 |
| B29457 | 36 | 49 | 52 |
| B29458 | 35 | 48 | 56 |
| B29459 | 41 | 56 | 69 |
| B29460 | 40 | 59 | 73 |
| B29461 | 46 | 66 | 66 |
| B29462 | 38 | 59 | 67 |
| B29463 | 38 | 55 | 62 |
| B29464 | 38 | 50 | 53 |
| B29465 | 37 | 51 | 51 |
| B29466 | 41 | 45 | 31 |
| B29467 | 34 | 56 | 65 |
| B29468 | 35 | 30 | 19 |
| B29469 | 48 | 59 | 64 |
| B29470 | 36 | 50 | 55 |
| B29471 | 41 | 47 | 39 |
| B29472 | 36 | 55 | 66 |
| B29473 | 35 | 40 | 66 |
| B29474 | 42 | 34 | 53 |
| B29475 | 44 | 61 | 63 |
| MEAN | 38 | 51 | 58 |
| S.D. | 5 | 9 | 13 |
| N | 25 | 25 | 25 |

F2 GENERATION

BODY WEIGHT CHANGE (Individual values/Grams/Males)

MALES Dose: 1000 mg/kg/day

| ANIMAL# | Day OF STUDY | | |
|---------|--------------|------|-------|
| | 1-8 | 8-15 | 15-22 |
| B29476 | 39 | 58 | 61 |
| B29477 | 47 | 60 | 76 |
| B29478 | 43 | 56 | 58 |
| B29479 | 47 | 63 | 61 |
| B29480 | 42 | 66 | 67 |
| B29481 | 35 | 56 | 59 |
| B29482 | 35 | 56 | 53 |
| B29483 | 35 | 50 | 46 |
| B29484 | 38 | 55 | 62 |
| B29485 | 41 | 52 | 66 |
| B29486 | 41 | 58 | 56 |
| B29487 | 28 | 35 | 44 |
| B29488 | 41 | 57 | 68 |
| B29489 | 41 | 65 | 74 |
| B29490 | 39 | 67 | 69 |
| B29491 | 39 | 57 | 64 |
| B29492 | 41 | 62 | 64 |
| B29493 | 34 | 55 | 63 |
| B29494 | 30 | 51 | 61 |
| B29495 | 38 | 68 | 71 |
| B29496 | 36 | 51 | 57 |
| B29497 | 10 | 43 | 54 |
| B29498 | 28 | 55 | 60 |
| B29499 | 41 | 65 | 65 |
| B29500 | 33 | 46 | 43 |
| MEAN | 37 | 56 | 61 |
| S.D. | 8 | 8 | 8 |
| N | 25 | 25 | 25 |

74. F2 generation - body weights (individual values/females/premating period)

F2 GENERATION

BODY WEIGHTS (Individual values/Grams/Females/Premating period)

FEMALES Dose: 0 mg/kg/day

| Animal No. | Day of STUDY | | | |
|------------|--------------|----|-----|-----|
| | 1 | 8 | 15 | 22 |
| B29801 | 57 | 93 | 144 | 194 |
| B29802 | 54 | 87 | 134 | 176 |
| B29803 | 52 | 80 | 116 | 151 |
| B29804 | 48 | 75 | 112 | 142 |
| B29805 | 50 | 80 | 118 | 148 |
| B29806 | 53 | 87 | 136 | 179 |
| B29807 | 57 | 99 | 156 | 205 |
| B29808 | 48 | 84 | 127 | 165 |
| B29809 | 46 | 78 | 120 | 158 |
| B29810 | 43 | 81 | 128 | 165 |
| B29811 | 56 | 87 | 129 | 171 |
| B29812 | 56 | 89 | 132 | 159 |
| B29813 | 57 | 92 | 133 | 170 |
| B29814 | 51 | 80 | 125 | 157 |
| B29815 | 50 | 84 | 128 | 166 |
| B29816 | 53 | 89 | 133 | 161 |
| B29817 | 40 | 74 | 117 | 151 |
| B29818 | 52 | 89 | 136 | 177 |
| B29819 | 52 | 92 | 138 | 168 |
| B29820 | 57 | 92 | 137 | 179 |
| B29821 | 63 | 98 | 137 | 169 |
| B29822 | 57 | 94 | 134 | 162 |
| B29823 | 57 | 89 | 130 | 166 |
| B29824 | 52 | 84 | 126 | 153 |
| B29825 | 50 | 86 | 131 | 164 |
| MEAN | 52 | 86 | 130 | 166 |
| S.D. | 5 | 7 | 10 | 14 |
| N | 25 | 25 | 25 | 25 |

F2 GENERATION

BODY WEIGHTS (Individual values/Grams/Females/Premating period)

FEMALES Dose: 250 mg/kg/day

| Animal No. | Day of STUDY | | | |
|------------|--------------|-----|-----|-----|
| | 1 | 8 | 15 | 22 |
| B29826 | 53 | 87 | 137 | 182 |
| B29827 | 44 | 74 | 115 | 150 |
| B29828 | 52 | 85 | 130 | 166 |
| B29829 | 62 | 100 | 153 | 187 |
| B29830 | 55 | 92 | 138 | 177 |
| B29831 | 63 | 102 | 146 | 186 |
| B29832 | 51 | 85 | 132 | 172 |
| B29833 | 58 | 92 | 133 | 173 |
| B29834 | 49 | 81 | 124 | 157 |
| B29835 | 53 | 85 | 131 | 162 |
| B29836 | 51 | 82 | 127 | 158 |
| B29837 | 50 | 85 | 128 | 165 |
| B29838 | 51 | 82 | 120 | 156 |
| B29839 | 47 | 77 | 115 | 150 |
| B29840 | 50 | 81 | 124 | 169 |
| B29841 | 47 | 77 | 121 | 161 |
| B29842 | 57 | 88 | 129 | 167 |
| B29843 | 52 | 87 | 125 | 159 |
| B29844 | 64 | 90 | 129 | 154 |
| B29845 | 53 | 83 | 120 | 156 |
| B29846 | 54 | 88 | 143 | 179 |
| B29847 | 55 | 91 | 146 | 172 |
| B29848 | 58 | 94 | 139 | 175 |
| B29849 | 54 | 82 | 116 | 148 |
| B29850 | 51 | 83 | 97 | 125 |
| MEAN | 53 | 86 | 129 | 164 |
| S.D. | 5 | 7 | 12 | 14 |
| N | 25 | 25 | 25 | 25 |

F2 GENERATION

BODY WEIGHTS (Individual values/Grams/Females/Premating period)

FEMALES Dose: 500 mg/kg/day

| Animal No. | Day of STUDY | | | |
|------------|--------------|-----|-----|-----|
| | 1 | 8 | 15 | 22 |
| B29851 | 49 | 78 | 116 | 155 |
| B29852 | 47 | 76 | 113 | 149 |
| B29853 | 45 | 74 | 115 | 157 |
| B29854 | 51 | 80 | 116 | 153 |
| B29855 | 53 | 92 | 140 | 177 |
| B29856 | 47 | 75 | 113 | 151 |
| B29857 | 52 | 84 | 121 | 153 |
| B29858 | 47 | 79 | 121 | 150 |
| B29859 | 47 | 76 | 105 | 141 |
| B29860 | 52 | 83 | 124 | 172 |
| B29861 | 61 | 100 | 146 | 184 |
| B29862 | 55 | 88 | 131 | 171 |
| B29863 | 51 | 87 | 129 | 162 |
| B29864 | 41 | 75 | 111 | 155 |
| B29865 | 50 | 87 | 127 | 151 |
| B29866 | 50 | 75 | 114 | 148 |
| B29867 | 41 | 67 | 101 | 132 |
| B29868 | 56 | 89 | 127 | 152 |
| B29869 | 63 | 98 | 146 | 181 |
| B29870 | 50 | 84 | 126 | 154 |
| B29871 | 66 | 107 | 149 | 185 |
| B29872 | 62 | 90 | 134 | 171 |
| B29873 | 57 | 94 | 151 | 187 |
| B29874 | 53 | 96 | 145 | 178 |
| B29875 | 59 | 96 | 149 | 178 |
| MEAN | 52 | 85 | 127 | 162 |
| S.D. | 7 | 10 | 15 | 15 |
| N | 25 | 25 | 25 | 25 |

F2 GENERATION

BODY WEIGHTS (Individual values/Grams/Females/Premating period)

FEMALES Dose: 1000 mg/kg/day

| Animal No. | Day of STUDY | | | |
|------------|--------------|----|-----|-----|
| | 1 | 8 | 15 | 22 |
| B29876 | 53 | 89 | 133 | 158 |
| B29877 | 55 | 86 | 123 | 150 |
| B29878 | 56 | 93 | 136 | 167 |
| B29879 | 58 | 97 | 144 | 177 |
| B29880 | 55 | 83 | 123 | 150 |
| B29881 | 57 | 89 | 131 | 168 |
| B29882 | 46 | 80 | 123 | 156 |
| B29883 | 49 | 78 | 119 | 150 |
| B29884 | 51 | 86 | 128 | 167 |
| B29885 | 55 | 88 | 129 | 156 |
| B29886 | 53 | 89 | 137 | 178 |
| B29887 | 47 | 70 | 104 | 145 |
| B29888 | 47 | 82 | 130 | 176 |
| B29889 | 55 | 82 | 117 | 147 |
| B29890 | 49 | 81 | 130 | 166 |
| B29891 | 51 | 82 | 116 | 142 |
| B29892 | 57 | 96 | 141 | 178 |
| B29893 | 51 | 85 | 141 | 179 |
| B29894 | 52 | 79 | 125 | 163 |
| B29895 | 56 | 89 | 132 | 171 |
| B29896 | 46 | 76 | 114 | 139 |
| B29897 | 44 | 74 | 116 | 154 |
| B29898 | 52 | 78 | 120 | 155 |
| B29899 | 53 | 89 | 137 | 166 |
| B29900 | 49 | 81 | 117 | 139 |
| MEAN | 52 | 84 | 127 | 160 |
| S.D. | 4 | 7 | 10 | 13 |
| N | 25 | 25 | 25 | 25 |

75. F2 generation - body weight change (individual values/grams/females/premating period)

F2 GENERATION

BODY WEIGHT CHANGE (Individual values/Grams/Females/Premating period)

FEMALES Dose: 0 mg/kg/day

| ANIMAL# | Day OF STUDY | | |
|---------|--------------|------|-------|
| | 1-8 | 8-15 | 15-22 |
| E29801 | 35 | 52 | 50 |
| E29802 | 33 | 47 | 42 |
| E29803 | 27 | 36 | 35 |
| E29804 | 26 | 37 | 30 |
| E29805 | 29 | 38 | 30 |
| E29806 | 35 | 49 | 43 |
| E29807 | 42 | 57 | 49 |
| E29808 | 36 | 43 | 38 |
| E29809 | 32 | 42 | 38 |
| E29810 | 37 | 48 | 37 |
| E29811 | 31 | 42 | 42 |
| E29812 | 33 | 43 | 27 |
| E29813 | 35 | 41 | 38 |
| E29814 | 30 | 45 | 32 |
| E29815 | 34 | 44 | 38 |
| E29816 | 36 | 44 | 27 |
| E29817 | 34 | 43 | 34 |
| E29818 | 37 | 47 | 41 |
| E29819 | 40 | 47 | 30 |
| E29820 | 35 | 45 | 42 |
| E29821 | 35 | 39 | 32 |
| E29822 | 38 | 40 | 28 |
| E29823 | 32 | 41 | 35 |
| E29824 | 32 | 42 | 27 |
| E29825 | 35 | 45 | 33 |
| MEAN | 34 | 44 | 36 |
| S.D. | 4 | 5 | 6 |
| N | 25 | 25 | 25 |

F2 GENERATION

BODY WEIGHT CHANGE (Individual values/Grams/Females/Premating period)

FEMALES Dose: 250 mg/kg/day

| ANIMAL# | Day OF STUDY | | |
|---------|--------------|------|-------|
| | 1-8 | 8-15 | 15-22 |
| B29826 | 34 | 50 | 45 |
| B29827 | 30 | 41 | 35 |
| B29828 | 33 | 45 | 35 |
| B29829 | 38 | 53 | 34 |
| B29830 | 37 | 46 | 39 |
| B29831 | 39 | 44 | 40 |
| B29832 | 33 | 47 | 40 |
| B29833 | 34 | 41 | 40 |
| B29834 | 32 | 43 | 32 |
| B29835 | 32 | 46 | 31 |
| B29836 | 31 | 45 | 31 |
| B29837 | 35 | 44 | 37 |
| B29838 | 31 | 37 | 36 |
| B29839 | 29 | 38 | 35 |
| B29840 | 30 | 43 | 45 |
| B29841 | 30 | 44 | 40 |
| B29842 | 32 | 41 | 37 |
| B29843 | 35 | 38 | 35 |
| B29844 | 26 | 38 | 26 |
| B29845 | 29 | 37 | 36 |
| B29846 | 34 | 55 | 37 |
| B29847 | 36 | 55 | 26 |
| B29848 | 36 | 44 | 37 |
| B29849 | 28 | 34 | 32 |
| B29850 | 33 | 14 | 28 |
| MEAN | 33 | 43 | 36 |
| S.D. | 3 | 8 | 5 |
| N | 25 | 25 | 25 |

F2 GENERATION

BODY WEIGHT CHANGE (Individual values/Grams/Females/Premating period)

FEMALES Dose: 500 mg/kg/day

| ANIMAL# | Day OF STUDY | | |
|---------|--------------|------|-------|
| | 1-8 | 8-15 | 15-22 |
| B29851 | 29 | 39 | 39 |
| B29852 | 29 | 37 | 36 |
| B29853 | 29 | 42 | 41 |
| B29854 | 29 | 36 | 37 |
| B29855 | 38 | 49 | 37 |
| B29856 | 29 | 37 | 38 |
| B29857 | 31 | 37 | 32 |
| B29858 | 31 | 43 | 29 |
| B29859 | 29 | 29 | 36 |
| B29860 | 32 | 40 | 48 |
| B29861 | 40 | 45 | 38 |
| B29862 | 34 | 43 | 40 |
| B29863 | 36 | 42 | 34 |
| B29864 | 33 | 36 | 45 |
| B29865 | 37 | 40 | 25 |
| B29866 | 25 | 39 | 35 |
| B29867 | 26 | 34 | 32 |
| B29868 | 33 | 38 | 25 |
| B29869 | 35 | 48 | 35 |
| B29870 | 34 | 42 | 28 |
| B29871 | 41 | 42 | 36 |
| B29872 | 28 | 44 | 37 |
| B29873 | 37 | 57 | 36 |
| B29874 | 43 | 49 | 33 |
| B29875 | 37 | 53 | 30 |
| MEAN | 33 | 42 | 35 |
| S.D. | 5 | 6 | 6 |
| N | 25 | 25 | 25 |

F2 GENERATION

BODY WEIGHT CHANGE (Individual values/Grams/Females/Premating period)

FEMALES Dose: 1000 mg/kg/day

| ANIMAL# | Day OF STUDY | | |
|---------|--------------|------|-------|
| | 1-8 | 8-15 | 15-22 |
| B29876 | 36 | 44 | 25 |
| B29877 | 31 | 38 | 26 |
| B29878 | 36 | 44 | 31 |
| B29879 | 39 | 48 | 33 |
| B29880 | 28 | 40 | 28 |
| B29881 | 32 | 43 | 37 |
| B29882 | 34 | 44 | 32 |
| B29883 | 30 | 41 | 31 |
| B29884 | 35 | 42 | 39 |
| B29885 | 33 | 41 | 28 |
| B29886 | 36 | 48 | 41 |
| B29887 | 23 | 34 | 41 |
| B29888 | 35 | 48 | 46 |
| B29889 | 27 | 35 | 30 |
| B29890 | 33 | 49 | 36 |
| B29891 | 30 | 34 | 26 |
| B29892 | 39 | 45 | 37 |
| B29893 | 34 | 56 | 39 |
| B29894 | 27 | 46 | 38 |
| B29895 | 33 | 44 | 39 |
| B29896 | 30 | 38 | 25 |
| B29897 | 30 | 42 | 38 |
| B29898 | 26 | 42 | 34 |
| B29899 | 37 | 47 | 29 |
| B29900 | 32 | 36 | 22 |
| MEAN | 32 | 43 | 33 |
| S.D. | 4 | 5 | 6 |
| N | 25 | 25 | 25 |

76. F2 generation - food consumption (individual values/grams per day/males)

F2 GENERATION

FOOD CONSUMPTION (Individual values/Grams per day/Males)

MALES Dose: 0 mg/kg/day

| Animal No. | Day of Study | | |
|------------|--------------|------|-------|
| | 1-8 | 8-15 | 15-22 |
| B29401 | 12 | 19 | 27 |
| B29402 | 15 | 21 | 28 |
| B29403 | 14 | 17 | 20 |
| B29404 | 13 | 17 | 22 |
| B29405 | 15 | 16 | 22 |
| B29406 | 15 | 20 | 25 |
| B29407 | 16 | 17 | 24 |
| B29408 | 14 | 17 | 25 |
| B29409 | 13 | 18 | 24 |
| B29410 | 15 | 21 | 29 |
| B29411 | 13 | 16 | 22 |
| B29412 | 15 | 17 | 23 |
| B29413 | 14 | 18 | 23 |
| B29414 | 7 | 18 | 22 |
| B29415 | 9 | 23 | 29 |
| B29416 | 11 | 17 | 24 |
| B29417 | 15 | 19 | 26 |
| B29418 | 16 | 18 | 24 |
| B29419 | 15 | 20 | 25 |
| B29420 | 16 | 20 | 26 |
| B29421 | 14 | 21 | 26 |
| B29422 | 14 | 19 | 25 |
| B29423 | 14 | 18 | 25 |
| B29424 | 15 | 18 | 24 |
| B29425 | 15 | 19 | 26 |
| MEAN | 14 | 19 | 25 |
| S.D. | 2 | 2 | 2 |
| N | 25 | 25 | 25 |

F2 GENERATION

FOOD CONSUMPTION (Individual values/Grams per day/Males)

MALES Dose: 250 mg/kg/day

| Animal No. | Day of Study | | |
|------------|--------------|------|-------|
| | 1-8 | 8-15 | 15-22 |
| B29426 | 14 | 19 | 22 |
| B29427 | 15 | 19 | 24 |
| B29428 | 16 | 20 | 26 |
| B29429 | 18 | 23 | 28 |
| B29430 | 19 | 16 | 25 |
| B29431 | 14 | 19 | 24 |
| B29432 | 16 | 19 | 24 |
| B29433 | 16 | 20 | 26 |
| B29434 | 29 | 15 | 26 |
| B29435 | 22 | 23 | 27 |
| B29436 | 16 | 19 | 25 |
| B29437 | 19 | 20 | 26 |
| B29438 | 13 | 15 | 20 |
| B29439 | 15 | 19 | 25 |
| B29440 | 13 | 16 | 23 |
| B29441 | 13 | 19 | 24 |
| B29442 | 13 | 17 | 23 |
| B29443 | 15 | 17 | 23 |
| B29444 | 16 | 19 | 24 |
| B29445 | 16 | 19 | 26 |
| B29446 | 14 | 19 | 25 |
| B29447 | 15 | 20 | 26 |
| B29448 | 16 | 21 | 28 |
| B29449 | 14 | 19 | 27 |
| B29450 | 15 | 20 | 27 |
| MEAN | 16 | 19 | 25 |
| S.D. | 3 | 2 | 2 |
| N | 25 | 25 | 25 |

F2 GENERATION

FOOD CONSUMPTION (Individual values/Grams per day/Males)

MALES Dose: 500 mg/kg/day

| Animal No. | Day of Study | | |
|------------|--------------|------|-------|
| | 1-8 | 8-15 | 15-22 |
| B29451 | 12 | 15 | 19 |
| B29452 | 13 | 17 | 25 |
| B29453 | 13 | 16 | 22 |
| B29454 | 17 | 21 | 26 |
| B29455 | 15 | 20 | 26 |
| B29456 | 13 | 16 | 22 |
| B29457 | 14 | 18 | 21 |
| B29458 | 15 | 17 | 22 |
| B29459 | 16 | 17 | 26 |
| B29460 | 16 | 19 | 27 |
| B29461 | 17 | 21 | 27 |
| B29462 | 15 | 19 | 25 |
| B29463 | 15 | 18 | 24 |
| B29464 | 13 | 16 | 22 |
| B29465 | 16 | 18 | 23 |
| B29466 | 14 | 19 | 14 |
| B29467 | 13 | 17 | 24 |
| B29468 | 15 | 17 | 12 |
| B29469 | 18 | 23 | 24 |
| B29470 | 14 | 17 | 22 |
| B29471 | 15 | 21 | 17 |
| B29472 | 15 | 18 | 25 |
| B29473 | 15 | 18 | 22 |
| B29474 | 14 | 18 | 17 |
| B29475 | 16 | 20 | 25 |
| MEAN | 15 | 18 | 22 |
| S.D. | 1 | 2 | 4 |
| N | 25 | 25 | 25 |

F2 GENERATION

FOOD CONSUMPTION (Individual values/Grams per day/Males)

MALES Dose: 1000 mg/kg/day

| Animal No. | Day of Study | | |
|------------|--------------|------|-------|
| | 1-8 | 8-15 | 15-22 |
| B29476 | 14 | 19 | 24 |
| B29477 | 17 | 22 | 29 |
| B29478 | 15 | 19 | 24 |
| B29479 | 17 | 22 | 26 |
| B29480 | 17 | 22 | 27 |
| B29481 | 15 | 19 | 25 |
| B29482 | 15 | 18 | 22 |
| B29483 | 14 | 17 | 20 |
| B29484 | 15 | 18 | 24 |
| B29485 | 15 | 20 | 25 |
| B29486 | 18 | 19 | 25 |
| B29487 | 12 | 13 | 18 |
| B29488 | 15 | 19 | 27 |
| B29489 | 17 | 21 | 28 |
| B29490 | 16 | 21 | 30 |
| B29491 | 16 | 19 | 26 |
| B29492 | 16 | 20 | 25 |
| B29493 | 14 | 18 | 25 |
| B29494 | 13 | 16 | 24 |
| B29495 | 16 | 20 | 28 |
| B29496 | 13 | 17 | 22 |
| B29497 | 6 | 14 | 19 |
| B29498 | 12 | 18 | 23 |
| B29499 | 14 | 21 | 27 |
| B29500 | 13 | 16 | 22 |
| MEAN | 15 | 19 | 25 |
| S.D. | 2 | 2 | 3 |
| N | 25 | 25 | 25 |

77. F2 generation - food consumption
(individual values/grams per day/females/premating period)

F2 GENERATION

FOOD CONSUMPTION (Individual values/Grams per day/Females/Premating period)

FEMALES Dose: 0 mg/kg/day

| Animal No. | Day of Study | | |
|------------|--------------|------|-------|
| | 1-8 | 8-15 | 15-22 |
| B29801 | 14 | 15 | 22 |
| B29802 | 12 | 17 | 20 |
| B29803 | 12 | 15 | 17 |
| B29804 | 12 | 15 | 17 |
| B29805 | 11 | 15 | 17 |
| B29806 | 13 | 17 | 20 |
| B29807 | 15 | 21 | 23 |
| B29808 | 13 | 17 | 19 |
| B29809 | 13 | 18 | 19 |
| B29810 | 14 | 17 | 20 |
| B29811 | 13 | 16 | 19 |
| B29812 | 13 | 16 | 17 |
| B29813 | 15 | 17 | 19 |
| B29814 | 13 | 16 | 18 |
| B29815 | 14 | 15 | 19 |
| B29816 | 12 | 17 | 19 |
| B29817 | 12 | 16 | 19 |
| B29818 | 14 | 19 | 20 |
| B29819 | 14 | 18 | 20 |
| B29820 | 13 | 17 | 20 |
| B29821 | 15 | 18 | 19 |
| B29822 | 15 | 16 | 18 |
| B29823 | 13 | 16 | 20 |
| B29824 | 13 | 15 | 18 |
| B29825 | 15 | 17 | 20 |
| MEAN | 13 | 17 | 19 |
| S.D. | 1 | 1 | 2 |
| N | 25 | 25 | 25 |

F2 GENERATION

FOOD CONSUMPTION (Individual values/Grams per day/Females/Premating period)

FEMALES Dose: 250 mg/kg/day

| Animal No. | Day of Study | | |
|------------|--------------|------|-------|
| | 1-8 | 8-15 | 15-22 |
| B29826 | 14 | 20 | 22 |
| B29827 | 12 | 16 | 19 |
| B29828 | 15 | 17 | 18 |
| B29829 | 25 | 18 | 20 |
| B29830 | 16 | 18 | 21 |
| B29831 | 15 | 17 | 20 |
| B29832 | 12 | 17 | 20 |
| B29833 | 14 | 16 | 18 |
| B29834 | 13 | 17 | 20 |
| B29835 | 14 | 17 | 19 |
| B29836 | 13 | 16 | 19 |
| B29837 | 13 | 16 | 19 |
| B29838 | 13 | 14 | 18 |
| B29839 | 13 | 14 | 17 |
| B29840 | 13 | 15 | 20 |
| B29841 | 12 | 15 | 19 |
| B29842 | 13 | 17 | 18 |
| B29843 | 14 | 16 | 19 |
| B29844 | 13 | 15 | 17 |
| B29845 | 15 | 14 | 17 |
| B29846 | 14 | 19 | 22 |
| B29847 | 15 | 19 | 21 |
| B29848 | 13 | 17 | 20 |
| B29849 | 14 | 15 | 16 |
| B29850 | 14 | 14 | 13 |
| MEAN | 14 | 16 | 19 |
| S.D. | 2 | 2 | 2 |
| N | 25 | 25 | 25 |

F2 GENERATION

FOOD CONSUMPTION (Individual values/Grams per day/Females/Premating period)

FEMALES Dose: 500 mg/kg/day

| Animal No. | Day of Study | | |
|------------|--------------|------|-------|
| | 1-8 | 8-15 | 15-22 |
| B29851 | 11 | 16 | 18 |
| B29852 | 11 | 15 | 17 |
| B29853 | 13 | 15 | 17 |
| B29854 | 12 | 15 | 16 |
| B29855 | 15 | 19 | 21 |
| B29856 | 12 | 15 | 17 |
| B29857 | 13 | 15 | 17 |
| B29858 | 14 | 17 | 19 |
| B29859 | 12 | 14 | 17 |
| B29860 | 14 | 15 | 19 |
| B29861 | 17 | 18 | 21 |
| B29862 | 14 | 17 | 22 |
| B29863 | 14 | 17 | 19 |
| B29864 | 14 | 14 | 18 |
| B29865 | 15 | 17 | 18 |
| B29866 | 11 | 14 | 18 |
| B29867 | 11 | 14 | 15 |
| B29868 | 13 | 15 | 17 |
| B29869 | 15 | 17 | 20 |
| B29870 | 13 | 16 | 18 |
| B29871 | 14 | 18 | 19 |
| B29872 | 12 | 16 | 20 |
| B29873 | 15 | 19 | 23 |
| B29874 | 16 | 19 | 20 |
| B29875 | 15 | 19 | 21 |
| MEAN | 13 | 16 | 19 |
| S.D. | 2 | 2 | 2 |
| N | 25 | 25 | 25 |

F2 GENERATION

FOOD CONSUMPTION (Individual values/Grams per day/Females/Premating period)

FEMALES Dose: 1000 mg/kg/day

| Animal No. | Day of Study | | |
|------------|--------------|------|-------|
| | 1-8 | 8-15 | 15-22 |
| B29876 | 15 | 18 | 19 |
| B29877 | 13 | 16 | 18 |
| B29878 | 14 | 17 | 18 |
| B29879 | 15 | 18 | 19 |
| B29880 | 13 | 15 | 17 |
| B29881 | 14 | 16 | 19 |
| B29882 | 14 | 16 | 18 |
| B29883 | 13 | 15 | 17 |
| B29884 | 10 | 18 | 20 |
| B29885 | 14 | 17 | 18 |
| B29886 | 16 | 19 | 22 |
| B29887 | 12 | 14 | 17 |
| B29888 | 14 | 17 | 23 |
| B29889 | 13 | 15 | 17 |
| B29890 | 15 | 18 | 22 |
| B29891 | 15 | 15 | 17 |
| B29892 | 14 | 18 | 21 |
| B29893 | 13 | 18 | 22 |
| B29894 | 12 | 16 | 19 |
| B29895 | 14 | 17 | 20 |
| B29896 | 19 | 15 | 16 |
| B29897 | 11 | 15 | 20 |
| B29898 | 13 | 15 | 18 |
| B29899 | 13 | 17 | 19 |
| B29900 | 13 | 16 | 17 |
| MEAN | 14 | 16 | 19 |
| S.D. | 2 | 1 | 2 |
| N | 25 | 25 | 25 |

78. F2 generation - sexual development

78.1. F2 generation - cleavage of the balanopreputial gland

F 2 GENERATION
CLEAVAGE OF THE BALANOPREPUTIAL GLAND
(observation between day 32 and day 47 old)

Sex: male

Dose-level: 0 mg/kg/day

| Animal No. | Age of animals (days) | Body weight on positive day (g) |
|------------------------|--------------------------|---------------------------------------|
| B29401 | 40 | 194.6 |
| B29402 | 41 | 211.7 |
| B29403 | 37 | 138.5 |
| B29404 | 35 | 127.9 |
| B29405 | 38 | 150.2 |
| B29406 | 34 | 136.1 |
| B29407 | 36 | 148.1 |
| B29408 | 38 | 157.2 |
| B29409 | 37 | 149.9 |
| B29410 | 35 | 156.3 |
| B29411 | 33 | 110.3 |
| B29412 | 35 | 141.1 |
| B29413 | 37 | 146.1 |
| B29414 | 36 | 151.3 |
| B29415 | 36 | 171.4 |
| B29416 | 36 | 130.3 |
| B29417 | 34 | 130.9 |
| B29418 | 35 | 141.0 |
| B29419 | 36 | 159.6 |
| B29420 | 36 | 161.7 |
| B29421 | 36 | 155.0 |
| B29422 | 33 | 131.3 |
| B29423 | 34 | 134.2 |
| B29424 | 35 | 138.5 |
| B29425 | 35 | 133.8 |
| n | 25 | 25 |
| Mean age of appearance | 36 | |
| Mean body weight | | 148.3 |
| SD | 2 | 21.5 |

F 2 GENERATION
CLEAVAGE OF THE BALANOPREPUTIAL GLAND
(observation between day 32 and day 47 old)

Sex: male

Dose-level: 250 mg/kg/day

| Animal No. | Age of animals (days) | Body weight on positive day (g) |
|------------------------|--------------------------|---------------------------------------|
| B29426 | 36 | 140.0 |
| B29427 | 35 | 137.1 |
| B29428 | 35 | 146.9 |
| B29429 | 34 | 164.7 |
| B29430 | 34 | 132.9 |
| B29431 | 34 | 134.5 |
| B29432 | 35 | 134.5 |
| B29433 | 36 | 162.1 |
| B29434 | 33 | 120.0 |
| B29435 | 35 | 134.8 |
| B29436 | 37 | 157.7 |
| B29437 | 33 | 125.5 |
| B29438 | 37 | 138.1 |
| B29439 | 36 | 149.3 |
| B29440 | 36 | 134.4 |
| B29441 | 34 | 133.5 |
| B29442 | 36 | 146.0 |
| B29443 | 33 | 125.4 |
| B29444 | 33 | 134.4 |
| B29445 | 34 | 134.0 |
| B29446 | 34 | 133.2 |
| B29447 | 34 | 141.5 |
| B29448 | 33 | 137.1 |
| B29449 | 35 | 146.9 |
| B29450 | 35 | 156.4 |
| n | 25 | 25 |
| Mean age of appearance | 35 | |
| Mean body weight | | 140.0 |
| SD | 1 | 11.0 |

F 2 GENERATION
CLEAVAGE OF THE BALANOPREPUTIAL GLAND
(observation between day 32 and day 47 old)

Sex: male

Dose-level: 500 mg/kg/day

| Animal No. | Age of animals (days) | Body weight on positive day (g) |
|------------------------|--------------------------|---------------------------------------|
| B29451 | 41 | 140.3 |
| B29452 | 37 | 146.7 |
| B29453 | 36 | 129.3 |
| B29454 | 34 | 147.6 |
| B29455 | 35 | 142.1 |
| B29456 | 36 | 133.5 |
| B29457 | 36 | 137.2 |
| B29458 | 35 | 124.8 |
| B29459 | 35 | 138.6 |
| B29460 | 33 | 123.9 |
| B29461 | 36 | 174.9 |
| B29462 | 37 | 154.8 |
| B29463 | 34 | 124.4 |
| B29464 | 37 | 139.1 |
| B29465 | 37 | 148.5 |
| B29466 | 32 | 120.1 |
| B29467 | 34 | 120.2 |
| B29468 | 33 | 124.2 |
| B29469 | 34 | 160.3 |
| B29470 | 38 | 156.3 |
| B29471 | 36 | 153.6 |
| B29472 | 35 | 143.8 |
| B29473 | 36 | 132.0 |
| B29474 | 35 | 138.5 |
| B29475 | 34 | 140.5 |
| n | 25 | 25 |
| Mean age of appearance | 35 | |
| Mean body weight | | 139.8 |
| SD | 2 | 14.0 |

F 2 GENERATION
CLEAVAGE OF THE BALANOPREPUTIAL GLAND
(observation between day 32 and day 47 old)

Sex: male

Dose-level: 1000 mg/kg/day

| Animal No. | Age of animals (days) | Body weight on positive day (g) |
|------------------------|--------------------------|---------------------------------------|
| B29476 | 36 | 157.3 |
| B29477 | 36 | 165.0 |
| B29478 | 34 | 136.6 |
| B29479 | 35 | 163.6 |
| B29480 | 35 | 152.5 |
| B29481 | 37 | 153.7 |
| B29482 | 38 | 156.7 |
| B29483 | 34 | 119.2 |
| B29484 | 35 | 136.2 |
| B29485 | 36 | 150.8 |
| B29486 | 33 | 123.7 |
| B29487 | 40 | 137.1 |
| B29488 | 38 | 179.4 |
| B29489 | 35 | 157.8 |
| B29490 | 34 | 139.8 |
| B29491 | 38 | 176.2 |
| B29492 | 34 | 139.1 |
| B29493 | 39 | 164.4 |
| B29494 | 37 | 142.8 |
| B29495 | 34 | 140.9 |
| B29496 | 34 | 123.9 |
| B29497 | 45 | 162.9 |
| B29498 | 36 | 134.6 |
| B29499 | 35 | 153.1 |
| B29500 | 36 | 130.4 |
| n | 25 | 25 |
| Mean age of appearance | 36 | |
| Mean body weight | | 147.9 |
| SD | 3 | 16.1 |

78.2. F2 generation - vaginal opening

F 2 GENERATION
VAGINAL OPENING
(observation between day 28 and day 40 old)

Sex: female

Dose-level: 0 mg/kg/day

| Animal No. | Age of animals (days) | Body weight on positive day (g) |
|------------------------|--------------------------|---------------------------------------|
| B29801 | 36 | 142.5 |
| B29802 | 35 | 128.5 |
| B29803 | 35 | 111.1 |
| B29804 | 46 | 149.8 |
| B29805 | 34 | 103.0 |
| B29806 | 36 | 136.8 |
| B29807 | 37 | 165.1 |
| B29808 | 37 | 136.3 |
| B29809 | 31 | 88.2 |
| B29810 | 34 | 114.4 |
| B29811 | 35 | 124.5 |
| B29812 | 31 | 99.5 |
| B29813 | 39 | 152.2 |
| B29814 | 34 | 112.3 |
| B29815 | 35 | 128.0 |
| B29816 | 39 | 147.2 |
| B29817 | 39 | 137.0 |
| B29818 | 32 | 111.3 |
| B29819 | 35 | 133.8 |
| B29820 | 33 | 117.2 |
| B29821 | 34 | 126.5 |
| B29822 | 30 | 100.8 |
| B29823 | 32 | 105.2 |
| B29824 | 34 | 111.8 |
| B29825 | 34 | 120.5 |
| n | 25 | 25 |
| Mean age of appearance | 35 | |
| Mean body weight | | 124.1 |
| SD | 3 | 19.4 |

F 2 GENERATION
VAGINAL OPENING
(observation between day 28 and day 40 old)

Sex: female

Dose-level: 250 mg/kg/day

| Animal No. | Age of animals (days) | Body weight on positive day (g) |
|------------------------|--------------------------|---------------------------------------|
| B29826 | 34 | 127.2 |
| B29827 | 33 | 97.0 |
| B29828 | 36 | 132.8 |
| B29829 | 37 | 159.1 |
| B29830 | 37 | 145.2 |
| B29831 | 33 | 124.9 |
| B29832 | 33 | 113.3 |
| B29833 | 32 | 110.9 |
| B29834 | 32 | 100.3 |
| B29835 | 34 | 118.1 |
| B29836 | 36 | 127.0 |
| B29837 | 31 | 97.1 |
| B29838 | 31 | 94.7 |
| B29839 | 36 | 113.0 |
| B29840 | 36 | 125.4 |
| B29841 | 36 | 121.5 |
| B29842 | 31 | 101.2 |
| B29843 | 32 | 105.0 |
| B29844 | 33 | 112.5 |
| B29845 | 36 | 121.6 |
| B29846 | 37 | 149.1 |
| B29847 | 34 | 129.4 |
| B29848 | 36 | 140.6 |
| B29849 | 34 | 113.1 |
| B29850 | 31 | 93.9 |
| n | 25 | 25 |
| Mean age of appearance | 34 | |
| Mean body weight | | 119.0 |
| SD | 2 | 17.2 |

F 2 GENERATION
VAGINAL OPENING
(observation between day 28 and day 40 old)

Sex: female

Dose-level:500 mg/kg/day

| Animal No. | Age of animals (days) | Body weight on positive day (g) |
|------------------------|--------------------------|---------------------------------------|
| B29851 | 33 | 97.5 |
| B29852 | 34 | 101.2 |
| B29853 | 33 | 96.5 |
| B29854 | 44 | 157.4 |
| B29855 | 32 | 111.1 |
| B29856 | 38 | 127.7 |
| B29857 | 39 | 137.2 |
| B29858 | 39 | 137.5 |
| B29859 | 31 | 85.5 |
| B29860 | 31 | 94.2 |
| B29861 | 31 | 112.8 |
| B29862 | 33 | 114.1 |
| B29863 | 34 | 113.8 |
| B29864 | 35 | 108.5 |
| B29865 | 36 | 127.6 |
| B29866 | 37 | 119.5 |
| B29867 | 34 | 89.9 |
| B29868 | 30 | 94.2 |
| B29869 | 33 | 126.1 |
| B29870 | 30 | 90.1 |
| B29871 | 30 | 110.7 |
| B29872 | 34 | 118.6 |
| B29873 | 33 | 123.5 |
| B29874 | 29 | 95.0 |
| B29875 | 31 | 114.4 |
| n | 25 | 25 |
| Mean age of appearance | 34 | |
| Mean body weight | | 112.2 |
| SD | 4 | 18.0 |

F 2 GENERATION
VAGINAL OPENING
(observation between day 28 and day 40 old)

Sex: female

Dose-level: 1000 mg/kg/day

| Animal No. | Age of animals (days) | Body weight on positive day (g) |
|------------------------|--------------------------|---------------------------------------|
| B29876 | 29 | 88.7 |
| B29877 | 33 | 107.3 |
| B29878 | 32 | 110.3 |
| B29879 | 30 | 105.0 |
| B29880 | 34 | 110.7 |
| B29881 | 34 | 118.3 |
| B29882 | 30 | 86.9 |
| B29883 | 32 | 96.6 |
| B29884 | 32 | 103.8 |
| B29885 | 32 | 107.2 |
| B29886 | 32 | 109.4 |
| B29887 | 34 | 93.2 |
| B29888 | 38 | 149.2 |
| B29889 | 33 | 103.4 |
| B29890 | 34 | 116.4 |
| B29891 | 32 | 96.2 |
| B29892 | 32 | 115.6 |
| B29893 | 33 | 113.5 |
| B29894 | 35 | 126.4 |
| B29895 | 34 | 120.8 |
| B29896 | 32 | 93.0 |
| B29897 | 36 | 121.0 |
| B29898 | 35 | 112.3 |
| B29899 | 34 | 122.5 |
| B29900 | 36 | 119.5 |
| n | 25 | 25 |
| Mean age of appearance | 33 | |
| Mean body weight | | 109.9 |
| SD | 2 | 13.8 |

79. F2 generation - individual necropsy observations

F2 GENERATION

INDIVIDUAL NECROPSY OBSERVATIONS

Dose: 0 mg/kg/day

| MALE# | ORGAN | OBSERVATION |
|--------|--------|---------------------------------|
| E29401 | | NO GROSS NECROPSY FINDINGS |
| E29402 | | NO GROSS NECROPSY FINDINGS |
| E29403 | | NO GROSS NECROPSY FINDINGS |
| E29404 | | NO GROSS NECROPSY FINDINGS |
| E29405 | KIDNEY | KIDNEY: DILATED PELVIS RIGHT |
| E29406 | | NO GROSS NECROPSY FINDINGS |
| E29407 | | NO GROSS NECROPSY FINDINGS |
| E29408 | | NO GROSS NECROPSY FINDINGS |
| E29409 | | NO GROSS NECROPSY FINDINGS |
| E29410 | | NO GROSS NECROPSY FINDINGS |
| E29411 | | NO GROSS NECROPSY FINDINGS |
| E29412 | | NO GROSS NECROPSY FINDINGS |
| E29413 | | NO GROSS NECROPSY FINDINGS |
| E29414 | | NO GROSS NECROPSY FINDINGS |
| E29415 | | NO GROSS NECROPSY FINDINGS |
| E29416 | | NO GROSS NECROPSY FINDINGS |
| E29417 | | NO GROSS NECROPSY FINDINGS |
| E29418 | | NO GROSS NECROPSY FINDINGS |

F2 GENERATION

INDIVIDUAL NECROPSY OBSERVATIONS

Dose: 0 mg/kg/day

| MALE# | ORGAN | OBSERVATION |
|--------|-------|----------------------------|
| B29419 | | NO GROSS NECROPSY FINDINGS |
| B29420 | | NO GROSS NECROPSY FINDINGS |
| B29421 | | NO GROSS NECROPSY FINDINGS |
| B29422 | | NO GROSS NECROPSY FINDINGS |
| B29423 | | NO GROSS NECROPSY FINDINGS |
| B29424 | | NO GROSS NECROPSY FINDINGS |
| B29425 | | NO GROSS NECROPSY FINDINGS |

F2 GENERATION
INDIVIDUAL NECROPSY OBSERVATIONS

Dose: 250 mg/kg/day

| MALE# | ORGAN | OBSERVATION |
|--------|-------|----------------------------|
| B29426 | | NO GROSS NECROPSY FINDINGS |
| B29427 | | NO GROSS NECROPSY FINDINGS |
| B29428 | | NO GROSS NECROPSY FINDINGS |
| B29429 | | NO GROSS NECROPSY FINDINGS |
| B29430 | | NO GROSS NECROPSY FINDINGS |
| B29431 | | NO GROSS NECROPSY FINDINGS |
| B29432 | | NO GROSS NECROPSY FINDINGS |
| B29433 | | NO GROSS NECROPSY FINDINGS |
| B29434 | | NO GROSS NECROPSY FINDINGS |
| B29435 | | NO GROSS NECROPSY FINDINGS |
| B29436 | | NO GROSS NECROPSY FINDINGS |
| B29437 | | NO GROSS NECROPSY FINDINGS |
| B29438 | | NO GROSS NECROPSY FINDINGS |
| B29439 | | NO GROSS NECROPSY FINDINGS |
| B29440 | | NO GROSS NECROPSY FINDINGS |
| B29441 | | NO GROSS NECROPSY FINDINGS |
| B29442 | | NO GROSS NECROPSY FINDINGS |
| B29443 | | NO GROSS NECROPSY FINDINGS |
| B29444 | | NO GROSS NECROPSY FINDINGS |

F2 GENERATION

INDIVIDUAL NECROPSY OBSERVATIONS

Dose: 250 mg/kg/day

| MALE# | ORGAN | OBSERVATION |
|--------|------------|---|
| B29445 | KIDNEY | KIDNEY: DILATED PELVIS RIGHT |
| B29446 | KIDNEY | KIDNEY: DILATED PELVIS RIGHT |
| B29447 | | NO GROSS NECROPSY FINDINGS |
| B29448 | INTESTINES | INTESTINES: DISTENDED WITH GAS Colon |
| B29449 | | NO GROSS NECROPSY FINDINGS |
| B29450 | | NO GROSS NECROPSY FINDINGS |

F2 GENERATION
INDIVIDUAL NECROPSY OBSERVATIONS

Dose: 500 mg/kg/day

| MALE# | ORGAN | OBSERVATION |
|--------|--------|---------------------------------|
| B29451 | | NO GROSS NECROPSY FINDINGS |
| B29452 | | NO GROSS NECROPSY FINDINGS |
| B29453 | | NO GROSS NECROPSY FINDINGS |
| B29454 | | NO GROSS NECROPSY FINDINGS |
| B29455 | | NO GROSS NECROPSY FINDINGS |
| B29456 | | NO GROSS NECROPSY FINDINGS |
| B29457 | KIDNEY | KIDNEY: DILATED PELVIS RIGHT |
| B29458 | | NO GROSS NECROPSY FINDINGS |
| B29459 | | NO GROSS NECROPSY FINDINGS |
| B29460 | | NO GROSS NECROPSY FINDINGS |
| B29461 | | NO GROSS NECROPSY FINDINGS |
| B29462 | | NO GROSS NECROPSY FINDINGS |
| B29463 | | NO GROSS NECROPSY FINDINGS |
| B29464 | | NO GROSS NECROPSY FINDINGS |
| B29465 | | NO GROSS NECROPSY FINDINGS |
| B29466 | | NO GROSS NECROPSY FINDINGS |
| B29467 | | NO GROSS NECROPSY FINDINGS |
| B29468 | KIDNEY | KIDNEY: DILATED PELVIS RIGHT |

F2 GENERATION

INDIVIDUAL NECROPSY OBSERVATIONS

Dose: 500 mg/kg/day

| MALE# | ORGAN | OBSERVATION |
|--------|-------|----------------------------|
| B29469 | | NO GROSS NECROPSY FINDINGS |
| B29470 | | NO GROSS NECROPSY FINDINGS |
| B29471 | | NO GROSS NECROPSY FINDINGS |
| B29472 | | NO GROSS NECROPSY FINDINGS |
| B29473 | | NO GROSS NECROPSY FINDINGS |
| B29474 | | NO GROSS NECROPSY FINDINGS |
| B29475 | | NO GROSS NECROPSY FINDINGS |

F2 GENERATION
INDIVIDUAL NECROPSY OBSERVATIONS

Dose: 1000 mg/kg/day

| MALE# | ORGAN | OBSERVATION |
|--------|--------|---------------------------------|
| B29476 | | NO GROSS NECROPSY FINDINGS |
| B29477 | | NO GROSS NECROPSY FINDINGS |
| B29478 | | NO GROSS NECROPSY FINDINGS |
| B29479 | KIDNEY | KIDNEY: DILATED PELVIS RIGHT |
| B29480 | | NO GROSS NECROPSY FINDINGS |
| B29481 | | NO GROSS NECROPSY FINDINGS |
| B29482 | | NO GROSS NECROPSY FINDINGS |
| B29483 | | NO GROSS NECROPSY FINDINGS |
| B29484 | | NO GROSS NECROPSY FINDINGS |
| B29485 | | NO GROSS NECROPSY FINDINGS |
| B29486 | | NO GROSS NECROPSY FINDINGS |
| B29487 | | NO GROSS NECROPSY FINDINGS |
| B29488 | | NO GROSS NECROPSY FINDINGS |
| B29489 | | NO GROSS NECROPSY FINDINGS |
| B29490 | | NO GROSS NECROPSY FINDINGS |
| B29491 | | NO GROSS NECROPSY FINDINGS |
| B29492 | | NO GROSS NECROPSY FINDINGS |
| B29493 | | NO GROSS NECROPSY FINDINGS |

F2 GENERATION

INDIVIDUAL NECROPSY OBSERVATIONS

Dose: 1000 mg/kg/day

| MALE# | ORGAN | OBSERVATION |
|--------|-------|----------------------------|
| B29494 | | NO GROSS NECROPSY FINDINGS |
| B29495 | | NO GROSS NECROPSY FINDINGS |
| B29496 | | NO GROSS NECROPSY FINDINGS |
| B29497 | | NO GROSS NECROPSY FINDINGS |
| B29498 | | NO GROSS NECROPSY FINDINGS |
| B29499 | | NO GROSS NECROPSY FINDINGS |
| B29500 | | NO GROSS NECROPSY FINDINGS |

F2 GENERATION
INDIVIDUAL NECROPSY OBSERVATIONS

Dose: 0 mg/kg/day

| FEMALE# | ORGAN | OBSERVATION |
|---------|---------------------------|---|
| B29801 | | NO GROSS NECROPSY FINDINGS |
| B29802 | | NO GROSS NECROPSY FINDINGS |
| B29803 | | NO GROSS NECROPSY FINDINGS |
| B29804 | | NO GROSS NECROPSY FINDINGS |
| B29805 | | NO GROSS NECROPSY FINDINGS |
| B29806 | | NO GROSS NECROPSY FINDINGS |
| B29807 | | NO GROSS NECROPSY FINDINGS |
| B29808 | | NO GROSS NECROPSY FINDINGS |
| B29809 | UTERUS | UTERUS: SEROUS CONTENTS IN UTERINE HORN BILATERAL |
| B29810 | | NO GROSS NECROPSY FINDINGS |
| B29811 | TRACHEA LUNGS LUNGS | TRACHEA: FOAMY CONTENTS LUNG: FOAMY CONTENTS LUNG: REDDISH COLOR |
| B29812 | | NO GROSS NECROPSY FINDINGS |
| B29813 | | NO GROSS NECROPSY FINDINGS |
| B29814 | | NO GROSS NECROPSY FINDINGS |
| B29815 | UTERUS UTERUS | UTERUS: SEROUS CONTENTS IN UTERINE HORN BILATERAL UTERUS: DILATATION OF UTERINE HORN BILATERAL |
| B29816 | | NO GROSS NECROPSY FINDINGS |

F2 GENERATION

INDIVIDUAL NECROPSY OBSERVATIONS

Dose: 0 mg/kg/day

| FEMALE# | ORGAN | OBSERVATION |
|---------|--------|--|
| B29817 | | NO GROSS NECROPSY FINDINGS |
| B29818 | | NO GROSS NECROPSY FINDINGS |
| B29819 | | NO GROSS NECROPSY FINDINGS |
| B29820 | | NO GROSS NECROPSY FINDINGS |
| B29821 | | NO GROSS NECROPSY FINDINGS |
| B29822 | | NO GROSS NECROPSY FINDINGS |
| B29823 | | NO GROSS NECROPSY FINDINGS |
| B29824 | | NO GROSS NECROPSY FINDINGS |
| B29825 | UTERUS | UTERUS: SEROUS CONTENTS IN UTERINE HORN BILATERAL |
| | UTERUS | UTERUS: DILATATION OF UTERINE HORN BILATERAL |

F2 GENERATION
INDIVIDUAL NECROPSY OBSERVATIONS

Dose: 250 mg/kg/day

| FEMALE# | ORGAN | OBSERVATION |
|---------|--------|--|
| B29826 | | NO GROSS NECROPSY FINDINGS |
| B29827 | | NO GROSS NECROPSY FINDINGS |
| B29828 | | NO GROSS NECROPSY FINDINGS |
| B29829 | | NO GROSS NECROPSY FINDINGS |
| B29830 | | NO GROSS NECROPSY FINDINGS |
| B29831 | UTERUS | UTERUS: SEROUS CONTENTS IN UTERINE HORN BILATERAL |
| B29832 | | NO GROSS NECROPSY FINDINGS |
| B29833 | | NO GROSS NECROPSY FINDINGS |
| B29834 | | NO GROSS NECROPSY FINDINGS |
| B29835 | | NO GROSS NECROPSY FINDINGS |
| B29836 | | NO GROSS NECROPSY FINDINGS |
| B29837 | | NO GROSS NECROPSY FINDINGS |
| B29838 | | NO GROSS NECROPSY FINDINGS |
| B29839 | | NO GROSS NECROPSY FINDINGS |
| B29840 | | NO GROSS NECROPSY FINDINGS |
| B29841 | | NO GROSS NECROPSY FINDINGS |
| B29842 | | NO GROSS NECROPSY FINDINGS |
| B29843 | | NO GROSS NECROPSY FINDINGS |

F2 GENERATION
INDIVIDUAL NECROPSY OBSERVATIONS

Dose: 250 mg/kg/day

| FEMALE# | ORGAN | OBSERVATION |
|---------|--------|--|
| B29844 | | NO GROSS NECROPSY FINDINGS |
| B29845 | | NO GROSS NECROPSY FINDINGS |
| B29846 | | NO GROSS NECROPSY FINDINGS |
| B29847 | | NO GROSS NECROPSY FINDINGS |
| B29848 | | NO GROSS NECROPSY FINDINGS |
| B29849 | | NO GROSS NECROPSY FINDINGS |
| B29850 | UTERUS | UTERUS: SEROUS CONTENTS IN UTERINE HORN BILATERAL |

F2 GENERATION
INDIVIDUAL NECROPSY OBSERVATIONS

Dose: 500 mg/kg/day

| FEMALE# | ORGAN | OBSERVATION |
|---------|--------|--|
| B29851 | | NO GROSS NECROPSY FINDINGS |
| B29852 | | NO GROSS NECROPSY FINDINGS |
| B29853 | | NO GROSS NECROPSY FINDINGS |
| B29854 | UTERUS | UTERUS: SEROUS CONTENTS IN UTERINE HORN BILATERAL |
| B29855 | | NO GROSS NECROPSY FINDINGS |
| B29856 | | NO GROSS NECROPSY FINDINGS |
| B29857 | UTERUS | UTERUS: SEROUS CONTENTS IN UTERINE HORN BILATERAL |
| B29858 | | NO GROSS NECROPSY FINDINGS |
| B29859 | | NO GROSS NECROPSY FINDINGS |
| B29860 | | NO GROSS NECROPSY FINDINGS |
| B29861 | | NO GROSS NECROPSY FINDINGS |
| B29862 | | NO GROSS NECROPSY FINDINGS |
| B29863 | | NO GROSS NECROPSY FINDINGS |
| B29864 | | NO GROSS NECROPSY FINDINGS |
| B29865 | | NO GROSS NECROPSY FINDINGS |
| B29866 | | NO GROSS NECROPSY FINDINGS |
| B29867 | UTERUS | UTERUS: SEROUS CONTENTS IN UTERINE HORN BILATERAL |

F2 GENERATION

INDIVIDUAL NECROPSY OBSERVATIONS

Dose: 500 mg/kg/day

| FEMALE# | ORGAN | OBSERVATION |
|---------|--------|--|
| B29868 | | NO GROSS NECROPSY FINDINGS |
| B29869 | | NO GROSS NECROPSY FINDINGS |
| B29870 | | NO GROSS NECROPSY FINDINGS |
| B29871 | LIVER | LIVER: BROWNISH NODULE(S) Papillary processus |
| | UTERUS | UTERUS: SEROUS CONTENTS IN UTERINE HORN BILATERAL |
| B29872 | | NO GROSS NECROPSY FINDINGS |
| B29873 | UTERUS | UTERUS: SEROUS CONTENTS IN UTERINE HORN BILATERAL |
| B29874 | | NO GROSS NECROPSY FINDINGS |
| B29875 | | NO GROSS NECROPSY FINDINGS |

F2 GENERATION
INDIVIDUAL NECROPSY OBSERVATIONS

Dose: 1000 mg/kg/day

| FEMALE# | ORGAN | OBSERVATION |
|---------|--------|--|
| B29876 | | NO GROSS NECROPSY FINDINGS |
| B29877 | | NO GROSS NECROPSY FINDINGS |
| B29878 | | NO GROSS NECROPSY FINDINGS |
| B29879 | | NO GROSS NECROPSY FINDINGS |
| B29880 | | NO GROSS NECROPSY FINDINGS |
| B29881 | | NO GROSS NECROPSY FINDINGS |
| B29882 | | NO GROSS NECROPSY FINDINGS |
| B29883 | | NO GROSS NECROPSY FINDINGS |
| B29884 | | NO GROSS NECROPSY FINDINGS |
| B29885 | | NO GROSS NECROPSY FINDINGS |
| B29886 | UTERUS | UTERUS: SEROUS CONTENTS IN UTERINE HORN BILATERAL |
| B29887 | | NO GROSS NECROPSY FINDINGS |
| B29888 | | NO GROSS NECROPSY FINDINGS |
| B29889 | | NO GROSS NECROPSY FINDINGS |
| B29890 | | NO GROSS NECROPSY FINDINGS |
| B29891 | | NO GROSS NECROPSY FINDINGS |
| B29892 | | NO GROSS NECROPSY FINDINGS |
| B29893 | | NO GROSS NECROPSY FINDINGS |

F2 GENERATION
INDIVIDUAL NECROPSY OBSERVATIONS

Dose: 1000 mg/kg/day

| FEMALE# | ORGAN | OBSERVATION |
|---------|--------|--|
| B29894 | | NO GROSS NECROPSY FINDINGS |
| B29895 | | NO GROSS NECROPSY FINDINGS |
| B29896 | | NO GROSS NECROPSY FINDINGS |
| B29897 | | NO GROSS NECROPSY FINDINGS |
| B29898 | | NO GROSS NECROPSY FINDINGS |
| B29899 | UTERUS | UTERUS: SEROUS CONTENTS IN UTERINE HORN BILATERAL |
| B29900 | UTERUS | UTERUS: SEROUS CONTENTS IN UTERINE HORN BILATERAL |

80. Study plan and amendments



ETHYL TERTIARY BUTYL ETHER (ETBE)
TWO-GENERATION STUDY
(REPRODUCTION AND FERTILITY EFFECTS)
BY THE ORAL ROUTE (GAVAGE) IN RATS

Test facility : CIT
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Study Number : 24859 RSR

Final study plan of 28 March 2003

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1. INTRODUCTION

1.1 Objective

The objective of this study is provide general information concerning the effects of the test item, ETHYL TERTIARY BUTYL ETHER (ETBE), on the integrity and performance of the male and female reproductive systems, including gonadal function, the estrous cycle, mating behavior, conception, gestation, parturition, lactation and weaning, and on the growth and development of the offspring.

1.2 Regulatory compliance

This study plan has been designed to comply with:

- OECD Guideline No. 416, 22nd January 2001,
- US EPA Guideline OPPTS 870.3800, August 1998,
- EC Commission Directive 87/302/EEC of Nov. 18, 1987.

The study will be conducted in compliance with the following Good Laboratory Practice regulations:

- OECD Principles on Good Laboratory Practice (as revised in 1997), ENV/MC/CHEM (98) 17,
- Commission Directive 1999/11/EC of 8 March 1999 adapting to technical progress the Principles of Good Laboratory Practice as specified in Council Directive 87/18/EEC on the harmonization of laws, regulations and administrative provisions relating to the application of the Principles of Good Laboratory Practice and the verification of their applications for tests on chemical substances (OJ No. L 77 of 23.3.1999),
- Décret N° 98-1312 du 31 décembre 1998 concernant les Bonnes Pratiques de Laboratoire (Journal Officiel du 1er janvier 1999), Ministère de l'Economie, des Finances et de l'Industrie,
- US Environmental Protection Agency, Federal Register, 40 CFR Part 792 ; Toxic Substances Control Act; Good Laboratory Practice Standards, August 17, 1989 (and subsequent amendments),
- Japanese Ministry of International Trade and Industry, Good Laboratory Practice Standards, Basic Industries Bureau, KanHogyo No. 39, March 31, 1984,
- Japanese Ministry of Health and Welfare, Good Laboratory Practice Standards, Pharmaceutical Affairs Bureau, YakuHatsu No. 229 and Environmental Agency, 59 KiKyoku No. 85, March 31, 1984.

The study will be conducted in compliance with Animal Health regulation, in particular:

- Council Directive No. 86/609/EEC of 24th November 1986 on the harmonization of laws, regulations or administrative provisions relating to the protection of animals used for experimental or other scientific purposes.

2. TEST AND CONTROL ITEMS

2.1 Identification

2.1.1 Test item

Name: ETHYL TERTIARY BUTYL ETHER (ETBE)

Synonyms: Ethyl-tert-Butyl Ether, ETBE, 2-ethoxy-2-methylpropane

CAS No.: 637-92-3

Batch No.: S02-08-159-I3 and S02-08-159-I3/2

Supplier: SEPAREX, Champigneulles, France

Description: colorless liquid

Purity: >98%

Impurities: ...(1)...

Storage conditions: at room temperature, in well-closed containers (flammable) in the dark

Expiry date: ...(1)...

Intended use: oxygenate additive for automotive fuels

Purity, composition, stability and expiry date which refer to the batch(es) to be used and handling conditions will be indicated in the test item data sheet (to be completed by the Sponsor). An analytical certificate will also be provided by the Sponsor.

Confirmation of identity of the test item is the responsibility of the Sponsor.

2.1.2 Vehicle

Name: corn oil (Sigma, Saint-Quentin-Fallavier, France)

Batch No.: will be documented in the raw data and specified in the study report

2.2 Dosage form preparation

The test item will be administered as a solution in the vehicle. The test item dosage forms will be prepared by the CIT Pharmacy once a week according to the demonstrated stability results obtained in a previous study: (*CIT/Study No. 24168 RSR*) and will be stored at room temperature (in a well closed bottle) in the dark prior to use. Each batch for each treatment level will be sub-divided into a suitable number of aliquots so that one bottle per dose per day will be opened for dosing, and the remainder discarded (after sampling, if necessary: see § 2.3 Chemical analysis of the dosage forms).

2.3 Chemical analysis of the dosage forms

2.3.1 Homogeneity

Before treatment, homogeneity of the dosing preparation will be confirmed at the lowest and highest concentrations prepared for use.

Duplicate samples will be taken from three levels (top, middle and bottom) with administration device to be used in the study, and analyzed for concentration of the test item.

2.3.2 Concentration

During the treatment period, a check of the concentrations will be performed on solutions of each control and test item dosage form prepared for use in weeks 1 and 2, and thereafter at 4 weekly intervals. All analyses will be performed by CIT, after using a method provided by the Sponsor. Aliquots will be taken from the remaining batches and stored frozen (-18°C) for possible future analysis.

(1) Will be specified by a study plan amendment.

3. TEST SYSTEM

3.1 Animals (F0 females)

Number: 200 rats (100 males and 100 females), designated F0 animals.

Strain and Sanitary status: Sprague-Dawley, CrI CD[®] (SD) IGS BR, Caesarian Obtained, Barrier Sustained-Virus Antibody Free (COBS-VAF[®]).

Reason for selection of species: the rat is a rodent species commonly accepted by regulatory authorities for this type of study and background data from previous studies is available at our laboratory.

Breeder: Charles River Laboratories France, l'Arbresle, France.

Age: at the beginning of the treatment period, the animals will be approximately 5 to 6 weeks old.

Acclimation: the animals will be acclimated for a period of at least 5 days before the beginning of the treatment period.

Allocation to groups: during the acclimation period, the required number of animals will be selected according to body weight and clinical condition and allocated to groups (by sex), according to a computerized stratification procedure, so that the average body weight of each group is similar.

Identification: the animals are individually identified by an ear tattoo (unique CIT identity number).

3.2 Environmental conditions

From arrival at CIT, the animals will be housed in a barriered rodent unit, under specific pathogen free (SPF) standard laboratory conditions.

The animal room conditions will be set as follows:

- temperature : $22 \pm 2^{\circ}\text{C}$,
- relative humidity : $50 \pm 20\%$,
- light/dark cycle : 12 h/12 h (07:00 - 19:00),
- ventilation : about 12 cycles/hour of filtered, non-recycled air.

The corresponding instrumentation and equipment are checked and calibrated at regular intervals. The temperature and relative humidity are recorded continuously and the records checked daily and filed.

The animal room will be disinfected before the arrival of the animals and then cleaned regularly thereafter.

3.3 Housing

The F0 animals will be housed individually in wire-mesh cages (43.0 x 21.5 x 18.0 cm). A metal tray containing autoclaved sawdust will be placed under each cage.

Prior to delivery and during lactation the F0 and F1 females will be housed individually in polycarbonate cages (43.0 x 21.5 x 20.0 cm) containing autoclaved sawdust (SICSA, Alfortville, France). Autoclaved wood shavings (SDS, Alfortville, France) will be provided as nesting material, a few days before delivery and during the lactation period.

After weaning, the F1 animals will be housed individually in wire-mesh cages (43.0 x 21.5 x 18.0 cm). A metal tray containing autoclaved sawdust will be placed under each cage.

The cages will be placed in numerical order on the racks. On a monthly basis, all the racks will be moved clockwise around the room, rack by rack. In this way, for each group, identical exposure to environmental conditions will be achieved.

3.4 Food and water

All animals will have free access to A04 C pelleted maintenance diet (SAFE, Villemoisson, Epinay-sur-Orge, France), distributed weekly and tap water (filtered with a 0.22 µm filter) contained in bottles.

3.5 Contaminant analyses

The batches of diet, sawdust and wood shavings are analyzed by the suppliers for composition and contaminant levels.

Bacterial and chemical analyses of water are performed regularly by external laboratories. These analyses include the detection of possible contaminants (pesticides, heavy metals and nitrosamines).

It is expected that no contaminants that may interfere with or prejudice the outcome of the study will be found in the diet, drinking water or sawdust.

4. TREATMENT (F0 animals)

4.1 Treatment groups

Rationale for dose-level selection

The dose-levels were selected by the Sponsor, following the results of a previously conducted study (CIT/Study No. 24168 RSR). In this previous reproduction/developmental dose-range finding study, except for a slight significant decrease on body weight in pregnant females at 1000 mg/kg/day and ptialism in most animals given 1000 mg/kg/day over the study, no effect on mating, pregnancy, lactation or litter data parameters was noted at 50, 250, 500 and 1000 mg/kg/day.

Consequently, dose-levels of 250, 500 and 1000 mg/kg/day were selected for this study. The treatment groups are detailed in the following table:

| Group | Number of animals | Dose-level (mg/kg/day) | Concentration (mg/mL) |
|-------|-------------------|------------------------|-----------------------|
| 1 | 25 males | 0 | 0 |
| | 25 females | | |
| 2 | 25 males | 250 | 62.5 |
| | 25 females | | |
| 3 | 25 males | 500 | 125 |
| | 25 females | | |
| 4 | 25 males | 1000 | 250 |
| | 25 females | | |

4.2 Duration

Each animal will be dosed once a day, at approximately the same time each day, 7 days a week, according to the following schedule:

- in the males:
 - 10 weeks before mating,
 - during the mating period (2 weeks),
 - until sacrifice (after weaning of the pups),
- in the females:
 - 10 weeks before mating,
 - during the mating period (2 weeks),
 - during pregnancy,
 - during lactation,
 - until sacrifice (after weaning of the pups).

Day 1 correspond to the first day of treatment period.

4.3 Administration

The oral route was selected based upon agreement with the Competent Authority requesting this study. It is also recommended by OECD Guideline 416, and was used in the preliminary range-finding study.

The dosage forms will be administered by gavage using a glass syringe fitted a metal gavage tube.

The quantity of the dosage form administered to each animal will be adjusted according to the most recently recorded body weight.

A constant dosage-volume of 4 mL/kg/day will be used.

Control animals (group 1) will receive the vehicle alone.

The dosage forms will be mixed regularly throughout the dosing procedure.

5. CLINICAL EXAMINATIONS OF F0 MALES AND FEMALES

5.1 Morbidity and mortality

Each animal will be checked at least twice a day for mortality and signs of morbidity (once during acclimation period and at least twice a day during the treatment period).

Any female showing signs of poor clinical condition, especially if death appears imminent, and any female having aborted, will be humanely killed.

Any female found dead or killed prematurely will be subjected to a macroscopic *post-mortem* examination.

5.2 Clinical signs

Each animal will be observed at two or three times a day, at approximately the same time (immediately after dosing, 1 hour and 4 hours post-dosing), for the recording of clinical signs (including evidence of physical or behavioural changes together with any signs of overt toxicity including abortion/resorption for the females).

The detailed and frequency of clinical observations are detailed below:

- study weeks 1 and 2 (pre-mating period): animals will be inspected for clinical signs three times per day (immediately post-dosing, 1 hour post-dosing, 4 hour post-dosing), 7 days per week,
- study weeks 3 and 4 (pre-mating period): if no clinical signs are apparent at the 1 hour or 4 hours observation period at the end of study week 2, the frequency of observations will be reduced to twice daily (immediately post-dosing, 1 hour post-dosing), 5 days per week (Monday to Friday) during study weeks 3 and 4. If clinical signs are present at this time, observations will be made following the schedule for study weeks 1 and 2,
- study weeks 5 to 9: if no clinical signs are apparent at the end of study week 4, routine observations will cease. If clinical signs are present at the end of study week 4, additional observations will be performed (1),
- study week 10 (one week before mating): the animals will be inspected for clinical signs twice daily (immediately post-dosing, 1 hour post-dosing), 7 days per week. If clinical signs are present at the 1 hour observations period, the animals will be observed again 4 hour post-dosing (1),
- gestation days 0 to 14 (pregnancy period): dams will be inspected three times per day (immediately post-dosing, 1 hour post-dosing, 4 hours post-dosing), 7 days per week,
- lactation days 1 - 14: dams will be inspected three times per day (immediately post-dosing, 1 hour post-dosing, 4 hours post-dosing), 7 days per week.

Observations recorded immediately post-dosing will be made while the animals are being handled. Observations made 1 hour and 4 hours post-dosing will be made with the animals in their cages.

This initial schedule may be modified by an amendment to the study plan in the event of any unexpected clinical findings, or if no relevant clinical signs are present.

On the other days, each animal will be observed at least once a day, at approximately the same time for recording of clinical signs.

5.3 Body weight

The body weight of each male will be recorded once a week until sacrifice.

The body weight of each female will be recorded once a week during the pre-mating and mating periods, then on days 0, 7, 14, 20 *post-coitum* and on days 1, 7, 14 and 21 *post-partum*.

5.4 Food consumption

The quantity of food consumed by each male will be recorded once a week until sacrifice.

The quantity of food consumed by each female will be recorded once a week during the pre-mating and mating periods, then over the following intervals:

- days 0-7, 7-14 and 14-20 *post-coitum*,
- days 1-7, 7-14 and 14-21 *post-partum*.

(1) Will be specified later by a study plan amendment.

6. MATING

6.1 Monitoring of estrous cycle

The estrous cycle stage will be determined from a fresh vaginal lavage (stained with methylene blue), each morning as follows:

- during the last three weeks of the pre-mating period,
- during the mating period, until the females are mated.

6.2 Mating procedure

Females will be paired with males from the same dose-level group: during the night one female will be placed with one male from an other litter of the same dose-level group, in order to avoid mating of one male and one female of the same litter.

Confirmation of mating will be made in the morning by checking the presence of a vaginal plug or of sperm in a vaginal lavage.

The day of confirmed mating will be designated day 0 *post-coitum* (p.c.).

Each female will be placed with the same male until mating occurs or 14 days have elapsed. The pre-coital time will be calculated for each pair.

7. PREGNANCY

After mating, each pair will be separated.

By the end of pregnancy, the females will be individually placed in appropriate cages with nesting material (see § 3.3 Housing).

Clinical monitoring will focus on any sign of abortion/resorption (bleeding) or premature delivery.

8. PARTURITION

Females will be allowed to litter normally and rear their progeny until weaning. Any sign of a difficult or prolonged parturition will be recorded.

The day of completed parturition will be designated day 1 *post-partum*. The length of gestation will be calculated.

9. OBSERVATIONS OF THE PROGENY OF THE F0 FEMALES DURING THE LACTATION PERIOD

Each pup will be identified individually on day 1 *post-partum*, by subcutaneous injection of Indian ink.

9.1 Litter size

The total litter size and numbers of pups of each sex will be recorded as soon as possible after birth.

The litters will be observed daily in order to note the number of live, dead and cannibalized pups.

Any gross malformation in pups will be noted.

9.2 Litter size adjustment

On day 4 *post-partum*, the size of each litter will be adjusted by randomly culling extra pups to obtain as nearly as possible four males and four females per litter. Whenever necessary, partial adjustment (for example five males and three females) will be permitted.

Standardization of litter size is considered to reduce the litter size-induced variability in the growth and development of the pups and thus increase the sensitivity of statistical analysis. This will also ensure that any adverse effects on pup growth and development are not masked by a treatment-related reduction in litter size.

9.3 Clinical signs

The pups will be observed daily for clinical signs.

9.4 Body weight

The weight of each pup will be recorded on days 1, 4, 7, 14 and 21 *post-partum*.

9.5 Anogenital distance

The anogenital distance (AGD) will be measured on day 1 *post-partum* for all pups of all groups.

An anogenital index will be calculated:
$$\frac{\text{AGD}}{\text{body weight}}$$

The ratio of AGD to the cube root of body weight will be also calculated.

9.6 Reflex development

The number of pups in each litter exhibiting the required characteristics of reflex development will be recorded at designated time-points:

- surface righting reflex : on day 5 *post-partum*,
- cliff avoidance : on day 11 *post-partum*,
- air-righting reflex : on day 17 *post-partum*.

10. TERMINAL SACRIFICE OF THE F0 GENERATION

Details about the examinations performed at terminal sacrifice of the F0 animals and their pups not selected for the F1 generation are given in § 20. Terminal examinations and pathology.

11. CONSTITUTION AND TREATMENT OF THE F1 GENERATION

On day 22 *post-partum*, one or two males and one or two females per litter (from as many litters as possible) will be selected to obtain 25 animals/sex/group and therefore constitute the F1 generation. Day 22 *post-partum* will be designated day 1 of the F1 generation.

F1 selected animals will be treated from day 1 (with the same procedure as for the F0 animals) throughout pre-mating, mating, pregnancy and until sacrifice (after weaning of their F2 progeny).

The experimental groups will be as follows:

| Group | Number of animals | Dose-level (mg/kg/day) | Concentration (mg/mL) |
|-------|------------------------|------------------------|-----------------------|
| 1 | 25 males 25 females | 0 | 0 |
| 2 | 25 males 25 females | 250 | 62.5 |
| 3 | 25 males 25 females | 500 | 125 |
| 4 | 25 males 25 females | 1000 | 250 |

12. CLINICAL EXAMINATIONS OF THE F1 GENERATION AFTER WEANING

12.1 Morbidity and mortality

Each animal will be checked at least twice a day for mortality and signs of morbidity.

Any female showing signs of poor clinical condition, especially if death appears imminent, and any female having aborted, will be humanely killed.

Any female found dead or killed prematurely will be subjected to a macroscopic *post-mortem* examination.

12.2 Clinical signs

- Each animal will be observed at least three times a day, at approximately the same time (immediately after dosing, 1 hour and 4 hours post-dosing) for the recording of clinical signs (including evidence of physical or behavioural changes together with any signs of overt toxicity including evidence of abortion/resorption for the females).

The detailed and frequency of clinical observations are detailed below:

- study weeks 1 and 2 (pre-mating period): animals will be inspected for clinical signs three times per day (immediately post-dosing, 1 hour post-dosing, 4 hour post-dosing), 7 days per week,
- study weeks 3 and 4 (pre-mating period): if no clinical signs are apparent at the 1 hour or 4 hours observation period at the end of study week 2, the frequency of observations will be reduced to twice daily (immediately post-dosing, 1 hour post-dosing), 5 days per week (Monday to Friday) during study weeks 3 and 4. If clinical signs are present at this time, observations will be made following the schedule for study weeks 1 and 2,
- study weeks 5 to 9: if no clinical signs are apparent at the end of study week 4, routine observations will cease. If clinical signs are present at the end of study week 4, additional observations will be performed (1),
- study week 10 (one week before mating): the animals will be inspected for clinical signs twice daily (immediately post-dosing, 1 hour post-dosing), 7 days per week. If clinical signs are present at the 1 hour observations period, the animals will be observed again 4 hour post-dosing (1),
- gestation days 0 to 14 (pregnancy period): dams will be inspected three times per day (immediately post-dosing, 1 hour post-dosing, 4 hours post-dosing), 7 days per week,
- lactation days 1 - 14: dams will be inspected three times per day (immediately post-dosing, 1 hour post-dosing, 4 hours post-dosing), 7 days per week.

Observations recorded immediately post-dosing will be made while the animals are being handled. Observations made 1 hour and 4 hours post-dosing will be made with the animals in their cages.

This initial schedule may be modified by an amendment to the study plan in the event of any unexpected clinical findings, or if no relevant clinical signs are present.

On the other days, each animal will be observed at least once a day, at approximately the same time for recording of clinical signs.

12.3 Body weight

The body weight of each male will be recorded once a week until sacrifice.

The body weight of each female will be recorded once a week during the pre-mating and mating periods, then on days 0, 7, 14, 20 *post-coitum* and on days 1, 7, 14, and 21 *post-partum*.

12.4 Food consumption

The quantity of food consumed by each male will be recorded once a week until sacrifice.

The quantity of food consumed by each female will be recorded once a week during the pre-mating and mating periods, then over the following intervals:

- days 0-7, 7-14 and 14-20 *post-coitum*,
- days 1-7, 7-14 and 14-21 *post-partum*.

(1) Will be specified later by a study plan amendment.

12.5 Sexual development

All male animals will be observed each day between day 32 and day 47 of age (i.e. day 11 and day 26 of F1 generation), until cleavage of the balanopreputial groove (preputial separation) is observed. Body weight will be recorded individually at that time.

All female animals will be observed each day when between day 28 and day 40 of age (i.e. day 7 and day 19 of F1 generation), until vaginal opening is observed. Body weight will be recorded individually at that time.

13. NEUROBEHAVIOURAL TESTS IN THE F1 GENERATION

13.1 Auditory function

When the animals are 4 weeks old, they will be tested for the acoustic startle response.

13.2 Pupil constriction

When the animals are 4 weeks old, they will be tested for the pupil constriction reflex.

13.3 Spontaneous locomotor activity

When the animals are between 7 and 8 weeks old, the spontaneous locomotor activity will be evaluated using an automated infra-red sensor equipment. Each animal will be tested twice at an interval of approximately 1 week. At each trial, the activity will be recorded over a 10-minute interval.

The following parameters will be recorded:

- movements within the front of the cage,
- movements within the back of the cage,
- back and forth movements.

14. MATING OF THE F1 GENERATION

14.1 Monitoring of estrous cycle

The estrous cycle stage will be determined from a fresh vaginal lavage (stained with methylene blue), each morning as follows:

- during the last 3 weeks of the pre-mating period,
- during the mating period, until the females are mated.

14.2 Mating procedure

When the animals are between 12 and 14 weeks old, females will be paired with males from the same dose-level group: during the night, one female will be placed with one male from another litter of the same dose-level group, in order to avoid mating of one male and one female of the same litter.

Confirmation of mating will be made in the morning by checking the presence of a vaginal plug or of sperm in a vaginal lavage.

The day of confirmed mating will be designated day 0 *post-coitum* (p.c.).

Each female will be placed with the same male until mating occurs or 14 days have elapsed.

The pre-coital time will be calculated for each pair.

15. PREGNANCY

After mating, each pair will be separated.

By the end of pregnancy, the females will be individually placed in appropriate cages with nesting material (see § 3.3 Housing).

Clinical monitoring will focus on any sign of abortion/resorption (bleeding) or premature delivery.

16. PARTURITION

Females will be allowed to litter normally and rear their progeny until weaning. Any sign of a difficult or prolonged parturition will be recorded.

The day of completed parturition will be designated day 1 *post-partum*. The length of gestation will be calculated.

17. OBSERVATIONS OF THE PROGENY OF THE F1 FEMALES DURING THE LACTATION PERIOD

Each pup will be identified individually on day 1 *post-partum*, by subcutaneous injection of Indian ink.

17.1 Litter size

The total litter size and numbers of pups of each sex will be recorded as soon as possible after birth.

The litters will be observed daily in order to note the number of live, dead and cannibalized pups.

Any gross malformation in pups will be noted.

17.2 Litter size adjustment

On day 4 *post-partum*, the size of each litter will be adjusted by randomly culling extra pups to obtain as nearly as possible four males and four females per litter. Whenever necessary, partial adjustment (for example five males and three females) will be permitted.

Standardization of litter size is considered to reduce the litter size-induced variability in the growth and development of the pups and thus increase the sensitivity of statistical analysis. This will also ensure that any adverse effects on pup growth and development are not masked by a treatment-related reduction in litter size.

17.3 Clinical signs

The pups will be observed daily for clinical signs.

17.4 Body weight

The weight of each pup will be recorded on days 1, 4, 7, 14 and 21 of *post-partum*.

17.5 Anogenital distance

The anogenital distance (AGD) will be measured on day 1 *post-partum* for all pups of all groups.

An anogenital index will be calculated:
$$\frac{\text{AGD}}{\text{body weight}}$$

The ratio of AGD to the cube root of body weight will be also calculated.

17.6 Reflex development

The number of pups in each litter exhibiting the required characteristics of reflex development will be recorded at designated time-points:

- surface righting reflex : on day 5 *post-partum*,
- cliff avoidance : on day 11 *post-partum*,
- air-righting reflex : on day 17 *post-partum*.

18. CONSTITUTION AND TREATMENT OF THE F2 GENERATION

On day 22 *post-partum*, one or two males and one or two females per litter (from as many litters as possible) will be selected to obtain 25 animals/sex/group and therefore constitute the F2 generation. Day 22 *post-partum* will be designated day 1 of the F1 generation.

F2 selected animals will be treated from day 1 until sexual maturity with the same procedure as for F0 and F1 animals.

The experimental groups will be as follows:

| Group | Number of animals | Dose-level (mg/kg/day) | Concentration (mg/mL) |
|-------|------------------------|------------------------|-----------------------|
| 1 | 25 males 25 females | 0 | 0 |
| 2 | 25 males 25 females | 250 | 62.5 |
| 3 | 25 males 25 females | 500 | 125 |
| 4 | 25 males 25 females | 1000 | 250 |

19. CLINICAL EXAMINATIONS OF THE F2 GENERATION AFTER WEANING

19.1 Morbidity and mortality

Each animal will be checked at least twice a day for mortality and signs of morbidity.

Any animal showing signs of poor clinical condition, especially if death appears imminent, will be humanely killed.

Any animal found dead or killed prematurely will be subjected to a macroscopic *post-mortem* examination.

19.2 Clinical signs

Each animal will be observed at least three times a day, at approximately the same time (immediately after dosing, 1 hour and 4 hours post-dosing) for the recording of clinical signs (including evidence of physical or behavioural changes together with any signs of overt toxicity including evidence of abortion/resorption for the females) from weaning until sexual maturity.

19.3 Body weight

The body weight of each male will be recorded once a week until sacrifice.

19.4 Food consumption

The quantity of food consumed by each male will be recorded once a week until sacrifice.

19.5 Sexual development

All male animals will be observed each day between day 32 and day 47 of age (i.e. day 11 and day 26 of F2 generation), until cleavage of the balanopreputial groove (preputial separation) is observed. Body weight will be recorded individually at that time.

All female animals will be observed each day when between day 28 and day 40 of age (i.e. day 7 and day 19 of F2 generation), until vaginal opening is observed.

Body weight will be recorded individually at that time.

20. TERMINAL EXAMINATIONS AND PATHOLOGY

20.1 Sacrifice

20.1.1 F0 animals and their progeny

All animals will be killed by asphyxiation using carbon dioxide and exsanguinated:

- F0 surviving males and females: after the weaning of F1 litters (between day 22 and day 25 *post-partum*),
- F0 females which have not delivered: after day 25 *post-coitum*,
- F0 females which did not mate: at least one week after the end of the mating period,
- pups not selected on day 4 or 22 *post-partum*: as appropriate,
- pups whose mother dies or mothers with litter dying entirely: as appropriate.

20.1.2 F1 animals and their progeny

All animals will be killed by asphyxiation using carbon dioxide and exsanguinated:

- F1 surviving males and females: after the weaning of each F2 litter (between day 22 and day 25 *post-partum*),
- F1 females which have not delivered: after day 25 *post-coitum*,
- F1 females which did not mate: at least one week after the end of the mating period,
- pups not selected on day 4 or 22 *post-partum*: as appropriate,
- pups whose mother dies or mothers with litter dying entirely: as appropriate.

20.1.3 F2 animals

All animals will be killed at sexual maturity by asphyxiation using carbon dioxide and exsanguination.

20.2 Organ weights

The body weight of all F0 and F1 animals killed at terminal sacrifice will be recorded and the following organs will be weighed (wet) as soon as possible after dissection:

- in all F0 and F1 males: testes (separately), epididymides (separately), prostate, seminal vesicles together with coagulating glands, brain, liver, kidneys, spleen, pituitary gland, thyroids with parathyroids and adrenals,
- in all F0 and F1 females: uterus, ovaries, brain, liver, kidneys, spleen, pituitary gland, thyroid and adrenals,
- in one F1 pup/sex/litter and one F2 pup/sex/litter: body weight, brain, spleen and thymus.

20.3 Seminology (F0 and F1 animals)

20.3.1 Epididymal sperm

Before sacrifice, each male will be slightly anesthetized (inhalation of isoflurane), and sperm will be sampled from the tail of the left epididymis (after weighing: see § 20.2 Organ weights) for investigation.

The animals will be then asphyxiated by carbon dioxide and exsanguinated.

20.3.1.1 Epididymal sperm motility

These investigations will be performed in all males of all the groups.

The sperm will be quickly evaluated on a slide, after appropriate dilution, and observation of 200 spermatozoa.

Results will be expressed as a proportion of motile and non-motile spermatozoa.

20.3.1.2 Epididymal sperm count and cauda sperm reserve

These investigations will be performed in all males of all the groups.

From a precisely measured sample of sperm, the spermatozoa will be counted, in a Malassez cell after appropriate dilution. Results will be expressed as a number of spermatozoa per mm³ of sperm.

Cauda sperm reserve will be derived from the number of sperm recovered by mincing the cauda tissue.

20.3.1.3 Epididymal sperm morphology

These investigations will be performed in all males of all groups. In the case of treatment-related changes, they will also be carried out in all males from all dose groups.

The morphology will be determined from a sperm smear, after eosin staining, and counting 100 spermatozoa per slide. Results will be expressed as a proportion of spermatozoa in each of the following categories:

- normal,
- normally shaped head separated from flagellum,
- mis-shapen head separated from flagellum,
- mis-shapen head with normal flagellum,
- mis-shapen head with abnormal flagellum,
- degenerative flagellar defect(s) with normal head,
- other flagellar defect(s) with normal head.

20.3.2 Testicular sperm

These investigations will be performed in all males of all groups. In the case of treatment-related changes, they will also be carried out in the males from all dose groups.

The left testis will be weighed and ground. The resulting preparation will be diluted and sperm heads resistant to homogeneization (i.e. elongated spermatids and mature spermatozoa) will be counted in a Neubauer cell.

Results will be expressed as a number of sperm heads per gram of testis and the daily sperm production rate will be calculated (using a time divisor of 6.10).

20.4 Macroscopic *post-mortem* examination

20.4.1 F0 and F1 animals

A macroscopic *post-mortem* examination of the principal thoracic and abdominal organs will be performed on all parent animals (F0 males and females, F1 males and females) including any that die during the study or are killed prematurely. In all F0 and F1 females, the number of implantation sites will be recorded and whenever appropriate will be classified as scars, late resorptions, live or dead fetuses.

In apparently non-pregnant or un-mated females, the presence of implantation scars on the uterus will be checked using ammonium sulphide staining technique.

In the case of delivery in females for which mating was not detected, the pups will be discarded.

Whenever necessary, photographs will be taken to document findings and kept with the study archives.

20.4.2 F2 animals

A macroscopic *post-mortem* examination of the principal thoracic and abdominal organs will be performed on all animals including any that die during the study or are killed prematurely.

20.4.3 Pups

A macroscopic *post-mortem* examination of the principal thoracic and abdominal organs will be performed on three pups/sex/litter of F0 females and F1 females killed at weaning. If any abnormalities are detected, an additional animal from the affected group will be sacrificed and subject to *post-mortem* examination in order to provide additional age- and treatment-matched control tissue.

Any pups that die during lactation, are killed prematurely, display clinical signs of toxicity or external abnormalities will also be subjected to a macroscopic *post-mortem* examination of the principal thoracic and abdominal organs.

At macroscopic *post-mortem* examination, organ weight of the pups (brain, spleen and thymus) will be removed and weighed (see § 20.2 Organ weights).

Other pups (e.g. not selected on day 4 or 21 *post-partum*) will not be examined.

20.5 Preservation of tissues

20.5.1 F0 and F1 animals

In all F0 and F1 animals, the following organs will be preserved in 10% buffered formalin (except for testes and epididymides which will be fixed in Bouin's fluid):

- macroscopic abnormalities,
- ovaries and oviducts,
- uterus (with cervix and horns),
- vagina,
- testis (right),
- epididymis (right),
- seminal vesicles,
- prostate,
- coagulating glands,
- pituitary gland,
- adrenal gland.

In addition, a vaginal smear will be taken from all F0 and F1 females and stained (using Harris Schorr's technique).

20.5.2 Pups

In all examined F0 and F1 pups, the macroscopic abnormalities will be preserved in 10% buffered formalin (except for testes and epididymides which will be fixed in Bouin's fluid).

20.6 Preparation of slides

All tissues required for microscopic examination will be embedded in paraffin wax, sectioned at a thickness of approximately 4 microns and stained with hematoxylin-eosin (except testes and epididymides which will be stained with hematoxylin/PAS).

Other specific staining will be made if necessary.

20.7 Microscopic examination

A microscopic examination will be performed at CIT as follows:

20.7.1 F0 and F1 animals

The following organs will be examined in the F0 and F1 animals of the control and high-dose groups:

- macroscopic abnormalities,
- ovaries and oviducts,
- uterus (with cervix and horns),
- vagina,
- testis*,
- epididymis,
- seminal vesicles,
- prostate,
- coagulating glands,
- pituitary gland,
- adrenal gland.

The following organs will be examined in the F0 and F1 animals of the low and intermediate-dose groups which are suspected to be un-fertile:

- ovaries*,
- uterus (with cervix and oviducts),
- vagina,
- testis*,
- epididymis,
- seminal vesicles,
- prostate,
- coagulating glands.

In addition, the vaginal smear taken at terminal sacrifice will be examined in all F0 and F1 females of all groups.

* In addition, a detailed histopathological examination will be conducted in order to:

- detect retained spermatids, missing germ cell layers or types, multinucleated giant cells or sloughing of spermatogenic cells into the lumen, in F0 and F1 males,
- detect qualitative depletion of the primordial follicle population in F0 and F1 females; evaluate quantitatively the primordial follicles (which can be combined with small growing follicles for comparison of treated and control ovaries) in F1 females.

If requested by the Sponsor and based upon the microscopic results of the high-dose group, other tissues of the low- and intermediate-dose groups will be examined (at additional cost).

21. ASSESSMENT OF DATA

Data will be expressed as group mean values \pm standard deviation (body weight, food consumption, implantations, fetuses, resorptions, pups, gestation length) or as proportions (pre-implantation loss, post-implantation loss, fetal observations, gestation index, live birth index, viability index). Whenever necessary, the experimental unit of comparison will be the litter.

The calculations will be performed for each group as follows:

Post-implantation loss:

$$\frac{\text{Number of implantation sites} - \text{Number of live concepti}}{\text{Number of implantations}} \times 100$$

Mating index:

$$\frac{\text{Number of mated animals}}{\text{Number of paired animals}} \times 100$$

Fertility index:

$$\frac{\text{Number of pregnant female partners}}{\text{Number of mated pairs}} \times 100$$

Gestation index:

$$\frac{\text{Number of females with live born pups}}{\text{Number of pregnant females}} \times 100$$

Live birth index:

$$\frac{\text{Number of live born pups}}{\text{Number of delivered pups}} \times 100$$

Viability index on day 4 *post-partum*:

$$\frac{\text{Number of surviving pups on day 4 } \textit{post-partum}}{\text{Number of live born pups}} \times 100$$

Lactation index:

$$\frac{\text{Number of surviving pups on day 21 } \textit{post-partum}}{\text{Number of surviving pups on day 4 } \textit{post-partum}} \times 100$$

22. STATISTICAL ANALYSIS

22.1 Data other than organ weights

Final interpretation of the numerical data will consider the results of statistical analysis along with other factors such as dose-response relationships and whether the results were toxicologically relevant in the light of other biological- and pathological findings.

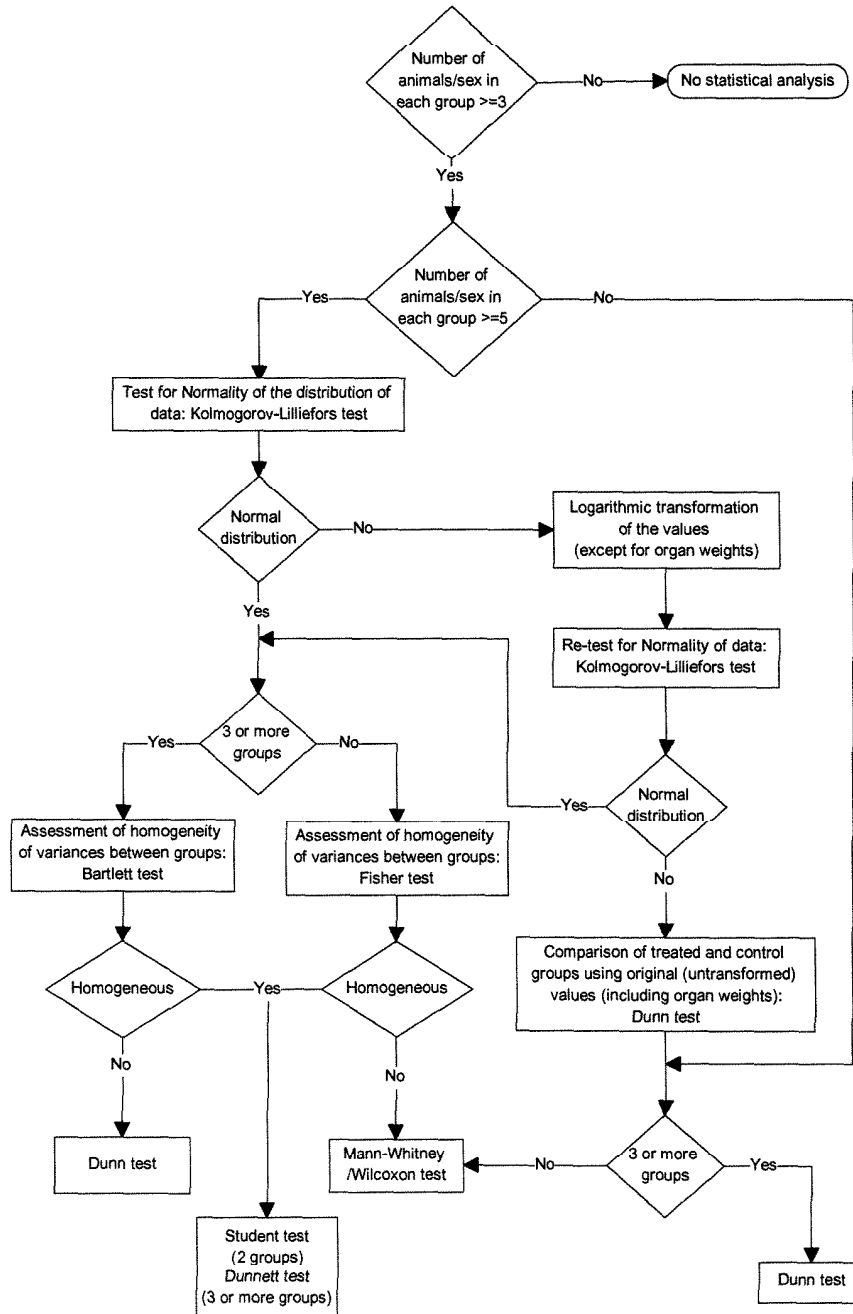
The litter will be the experimental unit for statistical analysis, with fetal body weight analyzed by sex as well as for both sexes combined.

In addition, the fetal body weights will be analyzed by a nested analysis of covariance (ANCOVA: fetal weights nested within dams nested within groups, with litter size as a covariant).

Other parameters will be evaluated for statistical significance using parametric or non-parametric methods, as appropriate. A detailed description of these statistical methods will be the subject of a specific amendment to the study plan.

22.2 Organ weights

The following sequence will be used for organ weight data:



23. BIBLIOGRAPHICAL REFERENCES

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- Dunn, J.O.: Multiple comparisons using rank sums. Technometrics 6 (3): 241-252 (1964).
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- Mann, H.B.; Whitney, D.R.: On a test of whether one of two random variables is stochastically larger than the other. Ann. Math. Statist. 18: 50-60 (1947).
- Salewski, (E.): Färbemethode zum makroskopischem Nachweis von Implantationstellen am Uterus der Ratte. Arch. Exp. Path. Pharmak., 247, 367 (1964).
- Seed, J. et al.: Methods for assessing sperm mobility, morphology and counts in the rat, rabbit and dog: a consensus report. Reprod. Toxicol., vol. 10, 3 237-244 (1996).
- Student, W.S.: The probable error of a mean. Biometrika 6 (1): 1-25 (1908).

24. AMENDMENTS TO THE STUDY PLAN

If necessary, amendments to the study plan will be made after discussion between the Study Director and the Study Monitor, and authorization by the Sponsor.

25. REPORTING

The Study Monitor will be informed of any significant findings at any time during the course of the study.

The final report in English (with a summary in French), will contain all data collected during the study. It will include sufficient information for compliance with the Guidelines listed in section 1.2 of this study plan.

Number of copies of the final report: seven (six bound + one unbound).

Proposed issue of the draft report: 13 weeks after completion of the last hysterectomy.

In the case of additional investigations being requested, the Study Monitor will be informed of any change in the delay of the report.

On issue of the final report, an electronic version will be provided as a PDF file (to include a copy of all signed pages, certificate of analysis and appendices)

26. QUALITY ASSURANCE UNIT

The study will be subjected to *Quality Assurance monitoring in order to ensure compliance with GLP, specifically:*

- (i) The study plan will be checked for compliance with GLP requirements.
- (ii) Specific and/or process-based inspections will be performed in order to ensure that the conduct of the study complies with Standard Operating Procedures.
- (iii) Data audit will be undertaken to ensure the reliability and integrity of the study data.
- (iv) The study report will be reviewed by the Quality Assurance Unit in order to ensure that the report faithfully reflects the data generated during the study and the study findings.

The dates on which the findings of critical inspections and reviews are reported to the Study Director and CIT management will be specified in the study report.

27. ARCHIVING

The following study materials will be retained in the archives of CIT (BP 563 – 27005 Evreux, France) for 10 years after the end of the *in vivo* phase of the study:

- study plan and possible amendments,
- raw data,
- correspondence,
- final report and possible amendments,
- tissues in preservative, blocks, histological slides (where appropriate),
- sample(s) of the test item,
- photographs (where appropriate).

On completion of this period, the archived study materials will be returned to the Sponsor, or may be archived at CIT for a further period (at additional cost).

The total duration of archiving (depending on regulations) will be the responsibility of the Sponsor.

In addition raw data not specific to the study, including but not limited to, certificates of analyses for food, water and bedding (if applicable) and records of environmental data and equipment calibration will also be archived by CIT for at least 30 years.

At the end of the study or utilization, all remaining test item (excluding the archive sample(s)) will be returned to the Sponsor unless otherwise stated by the Sponsor.

Unless otherwise requested by the study Sponsor, deep frozen specimens will be retained until acceptance of the final report by the Sponsor. Samples will then be disposed of unless prior instructions have been received from the Sponsor, requesting shipment of the samples or continued storage (at additional cost).

28. PROPOSED TIME SCHEDULE

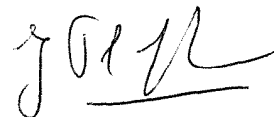
| | |
|---|------------------|
| Arrival of F0 animals (experimental starting date): | 25 March 2003 |
| First day of treatment: | 31 March 2003 |
| First day of delivery of F0 females: | 01 July 2003 |
| First day of F1 generation: | 23 July 2003 |
| First day of delivery of F1 females: | 23 October 2003 |
| Last day of necropsy of F1 animals (experimental completion date): | 13 December 2003 |
| Draft report: | 30 June 2003 |

In the case of relevant modification of the time schedule, the Study Monitor will be informed and the dates will be documented in the raw data and in the study report.

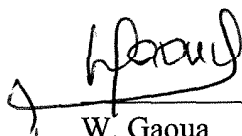
Study plan approved by:



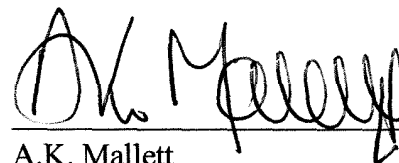
S. de Jouffrey or R. Forster
CIT Scientific Management
Date: 28 MAR . 2003



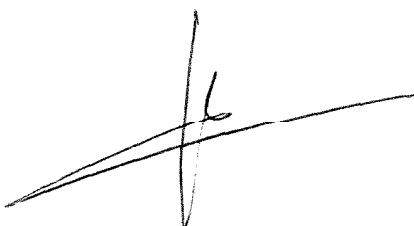
J.P. Gennart
Sponsor
Date: 28 mars 2003



W. Gaoua
CIT Study Director
Date: 28 Mar 2003



A.K. Mallett
Study Monitor
Date 28th March 2003



C. Galli-Kar
CIT Head of Quality Assurance Unit
Date: 28 Mar 2003

AMENDMENT TO STUDY PLAN

STUDY No.: 24859 RSR

SPONSOR: TOTALFINAELF

TEST ITEM: ETHYL TERTIARY BUTYL ETHER (ETBE)

STUDY TITLE: TWO-GENERATION STUDY (REPRODUCTION AND FERTILITY EFFECTS) BY THE ORAL ROUTE (GAVAGE) IN RATS

AMENDMENT No.: 1

Page 1/1

Justification: To correct typing errors (§ 20.3.1.3, 20.3.2, 20.4.3).

To reduce the frequency of clinical observation, in agreement with the Sponsor (§ 5.2).

Date of application: 31 March 2003 (First day of treatment) (§ 20.3.1.3, 20.3.2, 20.4.3).
11 April 2003 (§ 5.2).

5. CLINICAL EXAMINATIONS OF F0 MALES AND FEMALES

Amend the section according to the underlined and barred sentences:

5.2 Clinical signs

- study weeks 3 and 4 (prematuring period): ~~if no clinical signs are apparent at the 1 hour or 4 hours observation period at the end of study week 2, the frequency of observations will be reduced to twice daily (immediately post dosing, 1 hour post dosing), because no clinical signs were observed after 1 hour post-dosing, it was decided to not observe the animals at the 4 hour post-dosing,~~ 5 days per week (Monday to Friday) during study weeks 3 and 4. If clinical signs are ~~present at this time~~ become apparent, observations will be made following the schedule for study

20. TERMINAL EXAMINATIONS AND PATHOLOGY

Amend the sections according to the underlined and barred sentences:

20.3 Seminology (F0 and F1 animals)

20.3.1 Epididymal sperm

20.3.1.3 Epididymal sperm morphology

These investigations will be performed in all males of all groups. ~~In the case of treatment related changes, they will also be carried out in all males from all dose groups.~~

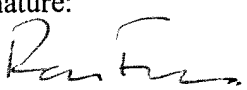
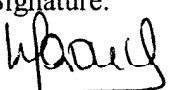
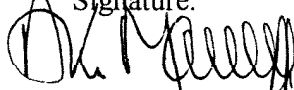
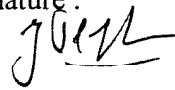
20.3.2 Testicular sperm

These investigations will be performed in all males of all groups. ~~In the case of treatment related changes, they will also be carried out in the males from all dose groups.~~

20.4 Macroscopic *post-mortem* examination

20.4.3 Pups

Any pups that die during lactation, or are killed prematurely, ~~display clinical signs of toxicity or external abnormalities~~ will also be subjected to a macroscopic *post-mortem* examination of the principal thoracic and abdominal organs.

| | | | |
|---|---|--|---|
| Scientific Management | Study Director | Study Monitor | Sponsor Representative |
| R. Forster or S. de Jouffrey | W. Gaoua | A.K. Mallet | J.P. Gennart |
| Date: 16 Apr. '03 | Date: 15 Apr 2003 | Date: 15 April 2003 | Date: 24 September 2003 |
| Signature: | Signature: | Signature: | Signature: |
|  |  |  |  |

AMENDMENT TO STUDY PLAN

STUDY No.: **24859 RSR**
 SPONSOR: **TOTALFINAELF**
 TEST ITEM: **ETHYL TERTIARY BUTYL ETHER (ETBE)**
 STUDY TITLE: **TWO-GENERATION STUDY (REPRODUCTION AND FERTILITY EFFECTS) BY THE ORAL ROUTE (GAVAGE) IN RATS**
 AMENDMENT No.: **2** Page 1/1

Justification: - to add information unavailable at the time of finalisation of the study plan

Date of application: 31 March 2003 (§ 19 first day of dosing)
 13 April 2003 (§ 2.1.1, first day of utilization of the batch No. 308 596)

Modify the following paragraph as indicated by the underlined words

2. TEST AND CONTROL ITEMS

2.1 Identification

2.1.1 Test item

Name: ETHYL TERTIARY BUTYL ETHER (purified ETBE)
Synonyms: Ethyl-tert-Butyl Ether, ETBE, 2-ethoxy-2-methylpropane
CAS No.: 637-92-3

Batch Nos.: S02-08-159-I3/1 (utilization from 27 2003 Mars to 30 April 2003)
and S02-08-159-I3/2 (utilization from 30 April 2003 to 6 August 2003)
and 308 596 (utilization since 13 August 2003)

Expiry date of the Batches Nos. S02-08-159-I3/1 and S02-08-159-I3/2: 25 September 2003
Expiry date of the Batch No. 308 596: 25 June 2004

Modify the following paragraph as indicated by the underlined sentences.

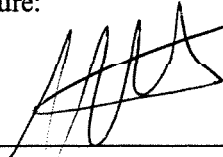
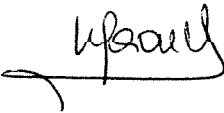
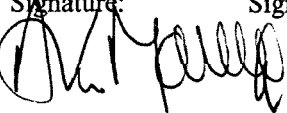

19. CLINICAL EXAMINATIONS OF THE F2 GENERATION AFTER WEANING

19.3 Body weight

The body weight of each animal will be recorded once a week until sacrifice.

19.4 Food consumption

The quantity of food consumed by each animal will be recorded once a week until sacrifice.

| | | | |
|--|--|---|--|
| Scientific Management | Study Director | Study Monitor | Sponsors Representative |
| S. de Jouffrey or R. Forster | W.Gaoua | A.K. Mallet | J.P. Gennart |
| Date: 07 Nov 2003 | Date: 7 Nov 2003 | Date: 13/11/03 | Date: 15/11/2003 |
| Signature:  | Signature:  | Signature:  | Signature:  |



AMENDMENT TO STUDY PLAN

STUDY No.: 24859 RSR

SPONSOR: TOTAL France SA

TEST ITEM: ETHYL TERTIARY BUTYL ETHER (ETBE)

STUDY TITLE: TWO-GENERATION STUDY (REPRODUCTION AND FERTILITY EFFECTS) BY THE ORAL ROUTE (GAVAGE) IN RATS

AMENDMENT No.: 3

Page 1/2

Justification: - at the request of the Sponsor, an interim draft report will be sent to the Sponsor.
- change the name of the Sponsor facility

Date of application: 20 January 2004 (§ 25)

From 06 May 2003 on, the Sponsor's company name is TOTAL France SA instead of TOTALFINAELF.

All sections of the study plan are modified accordingly.

Amend the following paragraph as indicated by the underlined words

25. REPORTING

The Study Monitor will be informed of any significant findings at any time during the course of the study.

The final report in English (with a summary in French), will contain all data collected during the study. It will include sufficient information for compliance with the Guidelines listed in section 1.2 of this study plan.

Number of copies of the final report: seven (six bound + one unbound).

Proposed issue of the draft report: 13 weeks after completion of the last hysterectomy.

An interim draft report, which will contain all F0 Generation data collected during the study, will be sent to the sponsor.

In the case of additional investigations being requested, the Study Monitor will be informed of any change in the delay of the report.

On issue of the final report, an electronic version will be provided as a PDF file (to include a copy of all signed pages, certificate of analysis and appendices)



AMENDMENT TO STUDY PLAN

STUDY No.: 24859 RSR

SPONSOR: TOTAL France SA

TEST ITEM: ETHYL TERTIARY BUTYL ETHER (ETBE)

STUDY TITLE: TWO-GENERATION STUDY (REPRODUCTION AND FERTILITY EFFECTS) BY THE ORAL ROUTE (GAVAGE) IN RATS

AMENDMENT No.: 3

Page 2/2

Amend the following paragraph as indicated by the underlined words

PROPOSED TIME SCHEDULE

| | |
|--|------------------------|
| Arrival of F0 animals | |
| (experimental starting date): | 25 March 2003 |
| First day of treatment: | 31 March 2003 |
| First day of delivery of F0 females: | 01 July 2003 |
| First day of F1 generation: | 23 July 2003 |
| First day of delivery of F1 females: | 23 October 2003 |
| Last day of necropsy of F1 animals | |
| (experimental completion date): | 13 December 2003 |
| <u>Interim draft report (F0 generation):</u> | <u>20 January 2004</u> |
| <u>Draft report (whole study):</u> | <u>12 May 2004</u> |

In the case of relevant modification of the time schedule, the Study Monitor will be informed and the dates will be documented in the raw data and in the study report.

| | | | |
|-----------------------|----------------|---------------|-------------------------|
| Scientific Management | Study Director | Study Monitor | Sponsors Representative |
|-----------------------|----------------|---------------|-------------------------|

S. de Jouffrey or R. Forster

W.Gaoua

A.K. Mallet

J.P. Gennart

Date: 15 Dec 2003

Date: 12 Dec 2003

Date: 19/12/03

Date : 23/01/2004

Signature:

Signature:

Signature:

Signature:



AMENDMENT TO STUDY PLAN

STUDY No.: 24859 RSR

SPONSOR: TOTAL France SA

TEST ITEM: ETHYL TERTIARY BUTYL ETHER (ETBE)

STUDY TITLE: **TWO-GENERATION STUDY (REPRODUCTION AND FERTILITY EFFECTS) BY THE ORAL ROUTE (GAVAGE) IN RATS**

AMENDMENT No.: 4

Page 1/2

Justification: additional examinations at request of the Sponsor

Date of application: 15 March 2004

Amend the following paragraph as indicated by the underlined words

20.7 Microscopic examination

A microscopic examination will be performed at CIT as follows:

20.7.1 F0 and F1 animals

The following organs will be examined in the F0 and F1 animals of the control and high-dose groups:

- macroscopic abnormalities,
- ovaries and oviducts,
- uterus (with cervix and horns),
- vagina,
- testis* (a),
- epididymis,
- seminal vesicles,
- prostate,
- coagulating glands,
- pituitary gland,
- adrenal gland.

(a) Based on the microscopic examination results of the control and high dose-group, the testis of all F1 males of the low and intermediate groups will be examined.

The following organs will be examined in the F0 and F1 animals of the low and intermediate-dose groups which are suspected to be un-fertile:

- ovaries*,
- uterus (with cervix and oviducts),
- vagina,
- testis*,
- epididymis,
- seminal vesicles,
- prostate,
- coagulating glands.

In addition, the vaginal smear taken at terminal sacrifice will be examined in all F0 and F1 females of all groups.

AMENDMENT TO STUDY PLAN

STUDY No.: 24859 RSR

SPONSOR: TOTAL France SA

TEST ITEM: ETHYL TERTIARY BUTYL ETHER (ETBE)

STUDY TITLE: **TWO-GENERATION STUDY (REPRODUCTION AND FERTILITY EFFECTS) BY THE ORAL ROUTE (GAVAGE) IN RATS**

AMENDMENT No.: 4

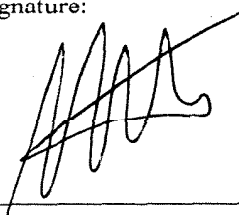
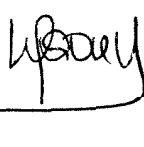
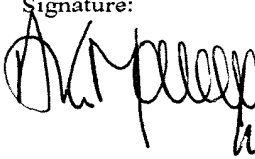
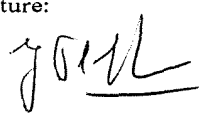
Page 2/2

* In addition, a detailed histopathological examination will be conducted in order to:

- detect retained spermatids, missing germ cell layers or types, multinucleated giant cells or sloughing of spermatogenic cells into the lumen, in F0 and F1 males,
- detect qualitative depletion of the primordial follicle population in F0 and F1 females; evaluate quantitatively the primordial follicles (which can be combined with small growing follicles for comparison of treated and control ovaries) in F1 females.

Delete the barred words

~~If requested by the Sponsor and based upon the microscopic results of the high-dose group, other tissues of the low- and intermediate-dose groups will be examined (at additional cost).~~

| | | | |
|---|---|--|---|
| Scientific Management | Study Director | Study Monitor | Sponsors Representative |
| S. de Jouffrey or R. Forster | W.Gaoua | A.K. Mallet | J.P. Gennart |
| Date: 15 Mar 2004 | Date: 15 Mar 2004 | Date: 26/03/04 | Date: 22/03/2004 |
| Signature: | Signature: | Signature: | Signature: |
|  |  |  |  |

AMENDMENT TO STUDY PLAN



STUDY No.: 24859 RSR

SPONSOR: TOTAL France SA

TEST ITEM: ETHYL TERTIARY BUTYL ETHER (ETBE)

STUDY TITLE: TWO-GENERATION STUDY (REPRODUCTION AND FERTILITY EFFECTS) BY THE ORAL ROUTE (GAVAGE) IN RATS

AMENDMENT No.: 5

Page 1/3

Justifications: . to add information unavailable at the time of finalization of the study plan,
. to correct typing errors.

Dates of application: 4 July 2003 (§ 2.3.1 and 2.3.2) and 31 March 2003 (§ 5, 12 and 22)

Complete the following paragraphs as indicated by the underlined words:

2. TEST AND CONTROL ITEMS

2.3 Chemical analysis of the dosage forms

2.3.1 Homogeneity

Before treatment, homogeneity of the dosing preparation for each batch of test item will be confirmed at the lowest and highest concentrations prepared for use.

[...]

2.3.2 Stability

A previous study performed with the test item batch No. S02-08-159-13 (CIT Study No. 24168 RSR) demonstrated satisfactory stability of the dosage forms (ETBE concentration in the range 1-333mg/mL) over a 9-day period at room temperature.

During the current study, the two dosage forms at 62.5 and 250 mg/mL prepared with the second batch of test item (308 596) will be sampled just after preparation and again after 4 and 9 days storage at room temperature. Each sample will be analyzed as soon as possible after sampling.

2.3.3 Concentration

[...]

3. TEST ITEM

[...]

. **Acclimation:** the animals will be acclimated for a period of at least 5 days before the beginning of the treatment period. A larger number of animals than necessary will be acclimated to permit selection and/or replacement of individuals. The animals may be supplied in several batches for logistical reasons.

AMENDMENT TO STUDY PLAN



STUDY No.: 24859 RSR

SPONSOR: TOTAL France SA

TEST ITEM: ETHYL TERTIARY BUTYL ETHER (ETBE)

STUDY TITLE: TWO-GENERATION STUDY (REPRODUCTION AND FERTILITY EFFECTS) BY THE ORAL ROUTE (GAVAGE) IN RATS

AMENDMENT No.: 5

Page 2/3

5. CLINICAL EXAMINATIONS OF F0 MALES AND FEMALES

5.4 Food consumption

The quantity of food consumed by each male will be recorded once a week until sacrifice.

The quantity of food consumed by each female will be recorded once a week during the pre-mating and mating period, then over the following intervals:

- . days 0-7, 7-14 and 14-20 *post-coitum*,
- . days 1-7, 7-14 and 14-21 *post-partum*.

No food consumption was noted during the pre-mating period.

12. CLINICAL EXAMINATIONS OF THE F1 GENERATION AFTER WEANING

12.4 Food consumption

[...]

The quantity of food consumed by each female will be recorded once a week during the pre-mating and mating period, then over the following intervals:

- . days 0-7, 7-14 and 14-20 *post-coitum*,
- . days 1-7, 7-14 and 14-21 *post-partum*.

No food consumption was noted during the pre-mating period.

AMENDMENT TO STUDY PLAN



STUDY No.: 24859 RSR

SPONSOR: TOTAL France SA

TEST ITEM: ETHYL TERTIARY BUTYL ETHER (ETBE)

STUDY TITLE: TWO-GENERATION STUDY (REPRODUCTION AND FERTILITY EFFECTS) BY THE ORAL ROUTE (GAVAGE) IN RATS

AMENDMENT No.: 5

Page 3/3

22. STATISTICAL ANALYSIS

22.1 Data other than organ weights

Mean values will be compared by one-way analysis of variance and Dunett's test (mean values being considered as normally distributed and variances being considered homogeneous).

Percentage values will be compared by the Fischer exact probability test. All the above statistics will be performed with a dedicated and validated computer system (Reprotox, version B1).

Mean percentages of motility and morphology sperm parameters will be Arcsine transformed and then compared by analysis variance.

Mean values for anogenital distance normalized to the cube root of pups body weight will be compared by analysis of variance.

These analysis will be performed using a dedicated commercial software package (Statview, version 5.0.1 SAS industries Inc).

Scientific Management

S. de Jouffrey or R. Forster

Date: 08 July 2004

Signature:

Study Director

W. Gaoua

Date: 08 July 2004

Signature:

Study Monitor

A.K. Mallett

Date:

Signature:

Sponsor's Representative

J.P. Gennart

Date:

Signature:
