

SUPPLEMENTARY MATERIALS
EHP 9666: OECD Validation of Rat Hershberger Assay: Phase-2 Dose Response Studies

These Supplementary Materials are arranged in 4 sections:

- I. A set of detailed data tables for the five mandatory sex accessory target tissues including means, standard deviations, coefficients of variation, and statistical significance for each laboratory as well as group calculations for each chemical dose group.
- II. A set of detailed data tables for the three optional tissues including means, standard deviations and statistical significance, for each laboratory and each chemical dose group.
- III. Comparison of the tissue LOELs for each test substance in Phase-2.
- IV. Benchmark dose calculations for the five mandatory sex accessory target tissues for each laboratory.

Section I. EHP 9666: OECD Validation of Rat Hershberger Assay: Phase-2 Dose Response Studies

A set of detailed data tables for the five mandatory sex accessory target tissues including means, standard deviations, coefficients of variation, and statistical significance for each laboratory as well as group calculations for each chemical dose group.

This section contains the following tables of detailed data for Phase-2 of the OECD Hershberger Validation Program.

Suppl. Material Table 1A. Methyltestosterone (MT) body weights, mandatory tissue weights and pooled statistics–stage-1 (mean \pm SD).

Suppl. Material Table 1B. Methyltestosterone (MT) body weights, mandatory tissue weights and pooled statistics –stage-2 (mean \pm SD).

Suppl. Material Table 2. Trenbolone (TREN) body weights, mandatory tissue weights and pooled statistics (mean \pm SD).

Suppl. Material Table 3A. Vinclozolin (VIN) body weights, mandatory tissue weights and pooled statistics - stage 1, 0.2 mg TP/kg-bw/d (mean \pm SD).

Suppl. Material Table 3B. Vinclozolin (VIN) body weights, mandatory tissue weights and pooled statistics - stage 2, 0.4 mg TP/kg-bw/d (mean \pm SD).

Suppl. Material Table 4A. *p,p'*-DDE (DDE) body weights, mandatory tissue weights and pooled statistics - stage-1, 0.2 mg TP/kg-bw/d (mean \pm SD).

Suppl. Material Table 4B. *p,p'*-DDE (DDE) body weights, mandatory tissue weights and pooled statistics - stage-2, 0.4 mg TP/kg-bw/d (mean \pm SD).

Suppl. Material Table 5. Procymidone (PRO) body weights, mandatory tissue weights and pooled statistics (mean \pm SD).

Suppl. Material Table 6. Linuron (LIN) body weights, mandatory tissue weights and pooled statistics (mean \pm SD).

Suppl. Material Table 7. Finasteride (FIN) body weights, mandatory tissue weights and pooled statistics (mean \pm SD).

Suppl Material Table 1A. Methyltestosterone (MT) body weights, mandatory tissue weights and pooled statistics–stage 1 (mean ± SD)

| Lab | Methyl Testosterone (mg/kg-bw/d) | 0 | 0.05 | 0.5 | 5 | 50 |
|-----|------------------------------------|---------------|---------------|--------------------------|------------------------------|-------------------------------|
| 11 | Starting Body Wt (g) ^a | 239.0 ± 10.17 | 238.0 ± 9.96 | 239.2 ± 6.99 | 239.4 ± 7.87 | 237.2 ± 8.83 |
| | Terminal Body Wt (g) ^a | 297.6 ± 19.06 | 291.2 ± 11.74 | 292.6 ± 10.85 | 294.6 ± 12.68 | 299.1 ± 15.28 |
| | Ventral prostate (mg) | 12.6 ± 5.57 | 14.4 ± 5.17 | 21.4 ± 7.78 [^] | 45.3 ± 8.79 ^{**^} | 128.3 ± 35.38 ^{**^} |
| | SVCG (mg) | 52.5 ± 12.48 | 50.2 ± 7.23 | 48.1 ± 12.96 | 70.7 ± 21.49 | 278.5 ± 65.88 ^{**^} |
| | LABC muscles (mg) | 236.3 ± 39.04 | 218.6 ± 38.49 | 228.7 ± 19.82 | 287.3 ± 19.17 ^{**^} | 533.8 ± 63.23 ^{**^} |
| | Glans penis (mg) | 48.9 ± 5.69 | 50.8 ± 3.14 | 49.9 ± 3.95 | 55.0 ± 4.48 ^{**} | 73.3 ± 5.34 ^{**^} |
| | Cowper's glands (mg) | 6.5 ± 2.50 | 6.8 ± 1.47 | 7.6 ± 1.80 | 11.0 ± 2.38 [^] | 27.2 ± 11.48 ^{**^} |
| 13 | Starting Body Wt (g) | 260.0 ± 9.66 | 259.8 ± 8.37 | 259.3 ± 8.23 | 259.8 ± 8.77 | 258.9 ± 8.86 |
| | Terminal Body Wt (g) | 309.2 ± 10.91 | 318.5 ± 16.53 | 313.4 ± 11.53 | 315.6 ± 17.62 | 317.0 ± 10.07 |
| | Ventral prostate (mg) | 21.1 ± 4.89 | 20.4 ± 3.16 | 18.7 ± 3.24 | 40.6 ± 14.58 ^{**^} | 135.0 ± 18.86 ^{**^} |
| | SVCG (mg) | 45.2 ± 6.05 | 43.7 ± 5.12 | 43.3 ± 4.91 | 65.7 ± 17.85 [^] | 248.2 ± 61.78 ^{**^} |
| | LABC muscles (mg) | 192.3 ± 28.59 | 198.0 ± 19.90 | 198.1 ± 15.71 | 253.2 ± 36.02 ^{**^} | 460.5 ± 52.65 ^{**^} |
| | Glans penis (mg) | 51.4 ± 2.83 | 55.6 ± 4.46 | 53.4 ± 4.83 | 64.8 ± 5.61 ^{**^} | 83.2 ± 6.60 ^{**^} |
| | Cowper's glands (mg) | 6.5 ± 1.54 | 7.8 ± 1.74 | 7.6 ± 1.8 | 10.8 ± 3.58 ^{**^} | 25.3 ± 1.12 ^{**^} |
| 15 | Starting Body Wt (g) | 222.1 ± 7.40 | 222.5 ± 9.01 | 225.5 ± 10.45 | 224.1 ± 8.77 | 221.1 ± 8.28 |
| | Terminal Body Wt (g) | 282.7 ± 17.81 | 288.6 ± 17.05 | 293.1 ± 15.21 | 290.4 ± 13.60 | 288.7 ± 11.71 |
| | Ventral prostate (mg) | 19.3 ± 1.89 | 22.1 ± 6.81 | 26.2 ± 4.16 | 51.1 ± 13.17 ^{**^} | 158.2 ± 35.19 ^{**^} |
| | SVCG (mg) | 44.2 ± 3.75 | 52.9 ± 23.80 | 66.2 ± 7.48 | 108.0 ± 23.28 ^{**^} | 312.6 ± 108.93 ^{**^} |
| | LABC muscles (mg) | 201.5 ± 23.25 | 203.6 ± 27.74 | 212.6 ± 30.14 | 254.2 ± 31.82 ^{**^} | 482.0 ± 78.02 ^{**^} |
| | Glans penis (mg) | 62.6 ± 4.47 | 60.8 ± 3.67 | 61.9 ± 4.66 | 74.4 ± 10.26 ^{**^} | 94.7 ± 11.58 ^{**^} |
| | Cowper's glands (mg) | 8.1 ± 1.39 | 7.5 ± 2.21 | 9.5 ± 1.8 | 11.8 ± 3.10 ^{**^} | 22.1 ± 2.72 ^{**^} |
| 16 | Starting Body Wt (g) | 227.4 ± 15.84 | 227.4 ± 10.13 | 227.8 ± 12.14 | 228.5 ± 15.05 | 227.3 ± 10.26 |
| | Terminal Body Wt (g) | 287.3 ± 16.12 | 286.0 ± 17.42 | 281.4 ± 16.92 | 293.4 ± 19.55 | 294.2 ± 16.46 |
| | Ventral prostate (mg) ^b | 19.2 ± 3.73 | 20.8 ± 5.08 | 19.5 ± 3.78 | 32.3 ± 10.44 | 150.9 ± 38.65 ^{**^} |
| | SVCG (mg) | 39.7 ± 4.82 | 37.3 ± 5.38 | 34.8 ± 5.67 | 41.2 ± 6.49 | 184.4 ± 15.57 ^{**^} |
| | LABC muscles (mg) | 206.3 ± 20.14 | 199.8 ± 32.16 | 203.6 ± 28.66 | 243.8 ± 27.83 ^{**} | 487.1 ± 26.36 ^{**^} |
| | Glans penis (mg) | 52.8 ± 2.53 | 53.1 ± 2.90 | 53.7 ± 1.52 | 56.8 ± 2.60 [*] | 83.5 ± 3.27 ^{**^} |
| | Cowper's glands (mg) ^b | 6.5 ± 0.65 | 7.4 ± 0.83 | 5.8 ± 0.9 | 7.6 ± 1.58 | 26.3 ± 5.16 ^{**^} |

R-square value (%)

OVR TRT LAB

Overall means and [CV] for tissues at a given dose

| | | | | | | | | |
|-----------------------|----|----|------|----------|----------|----------|-------------------------|-------------------------|
| Ventral prostate (mg) | 92 | 89 | 0.6 | 18 [29] | 19 [29] | 22 [26] | 42 [31] ^{**^} | 143 [23] ^{**^} |
| SVCG (mg) | 90 | 81 | 3.9 | 45 [19] | 46 [30] | 48 [29] | 71 [42] ^{**^} | 256 [32] ^{**^} |
| LABC (mg) | 92 | 90 | 7.8 | 209 [15] | 205 [14] | 211 [12] | 260 [12] ^{**^} | 491 [12] ^{**^} |
| Glans penis (mg) | 86 | 68 | 16.9 | 54 [13] | 55 [9] | 55 [11] | 63 [16] ^{**} | 84 [12] ^{**^} |
| Cowper's glands (mg) | 91 | 81 | 0.3 | 7 [25] | 7 [21] | 8 [27] | 10 [30] ^{**^} | 25 [25] ^{**^} |

SCVG – seminal vesicles and coagulating glands; OVR - Overall effect; TRT - Effect of treatments; LAB - Effect of laboratory; CV - Coefficient of variation.

^{*}, ^{**} Significantly different from control at P<0.05 and P<0.01, respectively, using T-test pairwise comparisons.

[^] Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with either starting or terminal body weight adjustment.

[#] Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with terminal body weight adjustment only.

^a The starting body weight is from the first day of substance administration and the terminal body weight is at necropsy approximately 24-hours after the last administration.

^b The VP and COWS were fixed and then weighed in laboratory 16

Suppl Material Table 1B. Methyltestosterone (MT) body weights, mandatory tissue weights and pooled statistics –stage 2 (mean ± SD)

| Lab | Methyl Testosterone (mg/kg-bw/d) | 0 | 0.5 | 2 | 10 | 40 |
|-----|-----------------------------------|---------------|---------------|------------------------------|------------------------------|-------------------------------|
| 2 | Starting Body Wt (g) ^a | 240.8 ± 12.42 | 242.5 ± 10.05 | 239.5 ± 13.17 | 238.8 ± 16.18 | 243.7 ± 9.44 |
| | Terminal Body Wt (g) ^a | 300.9 ± 22.51 | 306.9 ± 14.57 | 296.8 ± 13.38 | 303.6 ± 21.42 | 309.3 ± 11.41 |
| | Ventral prostate (mg) | 15.6 ± 5.53 | 17.5 ± 7.89 | 21.6 ± 11.34 | 50.3 ± 25.30 ^{**^} | 110.2 ± 34.88 ^{**^} |
| | SVCG (mg) | 53.4 ± 29.34 | 55.3 ± 15.86 | 45.0 ± 17.44 | 78.3 ± 38.61 | 142.0 ± 26.74 ^{**^} |
| | LABC muscles (mg) | 123.7 ± 26.73 | 112.6 ± 13.64 | 119.2 ± 22.44 | 159.2 ± 17.09 ^{**^} | 262.7 ± 23.12 ^{**^} |
| | Glans penis (mg) | 52.3 ± 6.92 | 55.2 ± 7.01 | 44.9 ± 12.72 | 68.1 ± 16.28 [*] | 79.2 ± 11.35 ^{**^} |
| | Cowper's glands (mg) | 5.9 ± 1.70 | 4.2 ± 1.05 | 6.4 ± 2.02 | 9.9 ± 4.78 | 19.0 ± 3.62 ^{**^} |
| 4 | Starting Body Wt (g) | 253.8 ± 12.91 | 255.3 ± 13.72 | 261.5 ± 13.56 | 256.7 ± 12.72 | 258.0 ± 15.62 |
| | Terminal Body Wt (g) | 321.7 ± 16.31 | 331.6 ± 19.72 | 334.0 ± 17.69 | 322.9 ± 15.57 | 323.3 ± 20.70 |
| | Ventral prostate (mg) | 24.8 ± 10.81 | 26.8 ± 5.97 | 50.5 ± 28.93 ^{**^} | 75.5 ± 9.33 ^{**^} | 162.5 ± 58.11 ^{**^} |
| | SVCG (mg) | 54.0 ± 10.63 | 64.0 ± 15.04 | 77.5 ± 15.66 ^{**} | 110.7 ± 27.48 ^{**^} | 246.5 ± 68.36 ^{**^} |
| | LABC muscles (mg) | 213.5 ± 33.78 | 214.1 ± 26.18 | 306.5 ± 71.62 ^{**^} | 326.6 ± 73.14 ^{**^} | 496.1 ± 80.63 ^{**^} |
| | Glans penis (mg) | 50.4 ± 6.71 | 56.9 ± 8.18 | 65.1 ± 9.82 ^{**^} | 66.6 ± 11.27 ^{**^} | 78.9 ± 11.00 ^{**^} |
| | Cowper's glands (mg) | 6.1 ± 1.85 | 7.2 ± 1.04 | 10.4 ± 3.58 ^{**^} | 13.2 ± 2.89 ^{**^} | 23.3 ± 5.97 ^{**^} |
| 6 | Starting Body Wt (g) | 234.1 ± 4.95 | 236.9 ± 10.73 | 234.7 ± 10.15 | 234.2 ± 14.50 | 234.3 ± 9.98 |
| | Terminal Body Wt (g) | 291.2 ± 7.49 | 302.0 ± 11.25 | 298.0 ± 16.33 | 293.5 ± 23.06 | 290.7 ± 14.88 |
| | Ventral prostate (mg) | 4.9 ± 3.24 | 4.2 ± 1.55 | 8.1 ± 4.74 | 21.1 ± 21.53 [*] | 70.0 ± 26.19 ^{**^} |
| | SVCG (mg) | 42.1 ± 21.42 | 43.4 ± 13.94 | 46.0 ± 13.61 | 83.9 ± 47.44 [*] | 190.9 ± 39.83 ^{**^} |
| | LABC muscles (mg) | 145.2 ± 37.51 | 166.2 ± 37.85 | 188.1 ± 13.02 [*] | 254.5 ± 73.36 ^{**^} | 445.9 ± 39.00 ^{**^} |
| | Glans penis (mg) | 60.4 ± 10.43 | 56.8 ± 12.74 | 67.2 ± 11.03 | 73.5 ± 20.31 | 88.4 ± 15.73 ^{**^} |
| | Cowper's glands (mg) | 0.7 ± 0.29 | 1.9 ± 1.78 | 2.3 ± 0.83 ^{**^} | 6.9 ± 5.78 ^{**^} | 17.4 ± 4.57 ^{**^} |
| 8 | Starting Body Wt (g) | 250.7 ± 5.49 | 251.0 ± 7.61 | 250.3 ± 6.06 | 249.3 ± 6.89 | 250.7 ± 9.68 |
| | Terminal Body Wt (g) | 319.6 ± 10.64 | 320.1 ± 15.70 | 313.5 ± 15.06 | 324.0 ± 12.37 | 321.4 ± 12.37 |
| | Ventral prostate (mg) | 18.8 ± 6.74 | 21.1 ± 2.32 | 24.8 ± 6.87 | 62.5 ± 14.13 ^{**^} | 151.1 ± 38.29 ^{**^} |
| | SVCG (mg) | 58.0 ± 20.02 | 62.2 ± 9.32 | 63.5 ± 14.09 | 117.0 ± 25.79 ^{**^} | 304.9 ± 111.25 ^{**^} |
| | LABC muscles (mg) | 187.7 ± 29.96 | 214.5 ± 34.69 | 229.5 ± 38.53 ^{*#} | 348.6 ± 57.91 ^{**^} | 523.8 ± 40.27 ^{**^} |
| | Glans penis (mg) | 50.5 ± 9.11 | 56.3 ± 12.43 | 52.7 ± 12.18 | 67.8 ± 12.45 ^{*#} | 90.3 ± 11.06 ^{**^} |
| | Cowper's glands (mg) | 6.8 ± 1.66 | 7.8 ± 2.48 | 11.8 ± 2.62 ^{**^} | 16.9 ± 1.91 ^{**^} | 29.9 ± 4.58 ^{**^} |

R-square (%)

OVR TRT LAB

| | OVR | TRT | LAB | Overall means and [CV] for tissues at a given dose | | | | | |
|-----------------------|-----|-----|-----|--|----------|------------------------|-------------------------|-------------------------|--|
| Ventral prostate (mg) | 77 | 50 | 29 | 16 [62] | 14 [58] | 26 [83] [*] | 52 [57] ^{**^} | 123 [43] ^{**^} | |
| SVCG (mg) | 75 | 67 | 8.6 | 52 [40] | 56 [28] | 58 [34] | 98 [39] ^{**^} | 221 [41] ^{**^} | |
| LABC (mg) | 82 | 53 | 33 | 168 [28] | 178 [29] | 211 [38] ^{**} | 272 [35] ^{**^} | 432 [26] ^{**^} | |
| Glans penis (mg) | 52 | 43 | 4.2 | 53 [17] | 56 [17] | 58 [25] | 69 [21] ^{**^} | 84 [15] ^{**^} | |
| Cowper's glands (mg) | 77 | 41 | 34 | 5 [59] | 5 [55] | 8 [57] ^{**^} | 12 [46] ^{**^} | 22 [30] ^{**^} | |

SCVG – seminal vesicles and coagulating glands; OVR - Overall effect; TRT - Effect of treatments; LAB - Effect of laboratory; CV - Coefficient of variation.

^{*}, ^{**} Significantly different from control at P<0.05 and P<0.01, respectively, using T-test pairwise comparisons.

[^] Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with either starting or terminal body weight adjustment.

[#] Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with terminal body weight adjustment only.

^a The starting body weight is from the first day of substance administration and the terminal body weight is at necropsy approximately 24-hours after the last administration.

Suppl Material Table 2. Trenbolone (TREN) body weights, mandatory tissue weights and pooled statistics (mean ± SD).

| Lab | Trenbolone (mg/kg-bw/d) | 0 | 0.3 | 1.5 | 8 | 40 |
|-----|-----------------------------------|---------------|---------------|---------------|-------------------------------|--------------------------------|
| 1 | Starting Body Wt (g) ^a | 192.7 ± 9.37 | 194.8 ± 7.20 | 196.3 ± 4.86 | 194.1 ± 7.90 | 192.2 ± 8.19 |
| | Terminal Body Wt (g) ^a | 207.4 ± 12.71 | 211.2 ± 14.91 | 209.4 ± 8.65 | 198.6 ± 9.22 | 189.7 ± 10.42* |
| | Ventral prostate (mg) | 15.7 ± 3.14 | 19.7 ± 5.02 | 18.8 ± 3.63 | 19.8 ± 4.27 | 37.6 ± 11.36 ** [^] |
| | SVCG (mg) | 23.2 ± 4.52 | 24.1 ± 11.50 | 26.1 ± 8.58 | 28.1 ± 11.11 | 58.0 ± 27.23 * ^{##} |
| | LABC muscles (mg) | 146.4 ± 18.30 | 137.2 ± 20.79 | 147.0 ± 26.23 | 165.1 ± 40.90 | 262.9 ± 41.55 ** [^] |
| | Glans penis (mg) | 42.9 ± 3.23 | 41.9 ± 3.93 | 44.7 ± 5.32 | 43.0 ± 6.90 | 52.2 ± 4.30 ** [^] |
| | Cowper's glands (mg) | 7.2 ± 2.61 | 5.8 ± 1.07 | 6.2 ± 0.99 | 6.6 ± 1.77 | 11.4 ± 3.75 * [^] |
| 3 | Starting Body Wt (g) | 201.1 ± 14.62 | 203.2 ± 11.40 | 205.9 ± 11.50 | 210.1 ± 9.24 | 207.4 ± 15.89 |
| | Terminal Body Wt (g) | 238.8 ± 17.47 | 243.4 ± 10.87 | 247.6 ± 19.25 | 236.9 ± 12.20 | 224.3 ± 23.93 |
| | Ventral prostate (mg) | 26.3 ± 13.38 | 29.9 ± 15.89 | 32.5 ± 15.29 | 29.4 ± 16.22 | 48.3 ± 22.55 * ^{##} |
| | SVCG (mg) | 63.0 ± 18.53 | 57.6 ± 9.28 | 76.6 ± 16.06 | 67.8 ± 30.94 | 155.5 ± 71.56 ** ^{##} |
| | LABC muscles (mg) | 195.6 ± 40.07 | 185.6 ± 36.53 | 218.7 ± 30.62 | 223.5 ± 36.83 | 395.2 ± 50.84 ** [^] |
| | Glans penis (mg) | 48.1 ± 3.63 | 48.0 ± 3.94 | 51.8 ± 5.83 | 51.3 ± 7.30 | 69.5 ± 11.34 ** [^] |
| | Cowper's glands (mg) | 5.7 ± 1.93 | 5.2 ± 1.26 | 7.3 ± 1.15 | 5.5 ± 0.69 | 11.2 ± 2.43 ** [^] |
| 7 | Starting Body Wt (g) | 245.9 ± 14.40 | 257.2 ± 12.15 | 248.3 ± 11.92 | 251.2 ± 13.08 | 251.8 ± 6.28 |
| | Terminal Body Wt (g) | 305.4 ± 20.86 | 327.3 ± 24.20 | 312.8 ± 11.86 | 303.6 ± 30.84 | 271.2 ± 16.02* |
| | Ventral prostate (mg) | 15.2 ± 5.41 | 19.5 ± 5.39 | 16.5 ± 6.11 | 25.3 ± 5.92 ** [^] | 35.2 ± 6.81 ** [^] |
| | SVCG (mg) | 95.4 ± 25.16 | 76.5 ± 23.20 | 73.4 ± 18.39 | 93.5 ± 14.20 | 170.6 ± 95.48 ** [^] |
| | LABC muscles (mg) | 233.5 ± 42.05 | 248.1 ± 57.69 | 260.3 ± 53.35 | 321.7 ± 57.23 ** [^] | 477.8 ± 74.51 ** [^] |
| | Glans penis (mg) | 69.7 ± 5.42 | 67.9 ± 5.18 | 65.1 ± 10.25 | 80.9 ± 5.19 * ^{##} | 87.3 ± 5.84 ** [^] |
| | Cowper's glands (mg) | 8.2 ± 3.52 | 10.3 ± 6.23 | 8.0 ± 2.86 | 10.0 ± 3.41 | 19.6 ± 9.00 ** [^] |

R-square (%)

OVR TRT LAB

| | OVR | TRT | LAB | Overall means and [CV] for tissues at a given dose | | | | |
|-----------------------|-----|-----|-----|--|----------|----------|---------------------------|--------------------------|
| Ventral prostate (mg) | 45 | 32 | 11 | 19 [50] | 23 [47] | 23 [52] | 25 [42] * | 40 [33] ** [^] |
| SVCG (mg) | 46 | 18 | 57 | 61 [58] | 53 [51] | 59 [47] | 63 [54] | 128 [66] ** [^] |
| LABC (mg) | 71 | 44 | 37 | 192 [26] | 191 [32] | 209 [29] | 237 [33] ** ^{##} | 379 [28] ** [^] |
| Glans penis (mg) | 62 | 16 | 66 | 54 [24] | 53 [23] | 54 [21] | 58 [31] | 70 [24] ** [^] |
| Cowper's glands (mg) | 46 | 33 | 15 | 7 [63] | 7 [59] | 7 [27] | 7 [39] | 14 [48] ** [^] |

SCVG – seminal vesicles and coagulating glands; OVR – Overall effect on tissue; TRT - Effect of treatments; LAB - Effect of laboratory; CV - Coefficient of variation.

*, ** Significantly different from control at P<0.05 and P<0.01, respectively, using T-test pairwise comparisons.

[^] Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with either starting or terminal body weight adjustment.

[#] Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with terminal body weight adjustment only.

^{##} Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with starting body weight adjustment only.

^a The starting body weight is from the first day of substance administration and the terminal body weight is at necropsy approximately 24-hours after the last administration.

Suppl Material Table 3A. Vinclozolin (VIN) body weights, mandatory tissue weights and pooled statistics - stage 1, 0.2 mg TP/kg-bw/d (mean ± SD).

| Lab | Testosterone Propionate (mg/kg-bw/d) | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 |
|-----|--------------------------------------|---------------|------------------|-------------------|-------------------|-------------------|
| | Vinclozolin (mg/kg-bw/d) | 0 | 3 | 10 | 30 | 100 |
| 10 | Starting Body Wt (g) ^a | 232.8 ± 6.77 | 233.1 ± 7.93 | 232.9 ± 9.63 | 232.9 ± 7.07 | 231.4 ± 6.73 |
| | Terminal Body Wt (g) ^a | 291.2 ± 6.73 | 289.9 ± 6.69 | 286.2 ± 12.68 | 286.3 ± 14.62 | 289.2 ± 11.56 |
| | Ventral prostate (mg) | 106.4 ± 14.26 | 98.9 ± 21.14 | 84.1 ± 13.72 ** | 75.3 ± 1.31 ** | 38.9 ± 13.18 **^ |
| | SVCG (mg) | 216.7 ± 38.21 | 221.6 ± 16.72 | 168.4 ± 42.77 | 116.2 ± 20.78 **^ | 47.3 ± 15.09 **^ |
| | LABC muscles (mg) | 361.3 ± 46.54 | 320.6 ± 41.20 | 323.9 ± 19.29 | 268.0 ± 23.87 **^ | 181.8 ± 34.78 **^ |
| | Glans penis (mg) | 70.1 ± 3.88 | 69.9 ± 1.98 | 67.3 ± 3.97 | 64.7 ± 4.48 ** | 51.4 ± 6.59 **^ |
| | Cowper's glands (mg) | 20.8 ± 1.29 | 21.1 ± 5.3 | 19.5 ± 3.49 | 15.1 ± 2.87 **^ | 7.4 ± 1.75 **^ |
| 11 | Starting Body Wt (g) | 247.6 ± 8.96 | 246.7 ± 8.10 | 245.2 ± 10.72 | 246.2 ± 5.91 | 245.9 ± 8.33 |
| | Terminal Body Wt (g) | 326.8 ± 11.23 | 327.7 ± 9.75 | 320.8 ± 15.11 | 319.6 ± 14.03 | 319.1 ± 17.51 |
| | Ventral prostate (mg) | 97.2 ± 42.65 | 111.6 ± 18.27 | 105.1 ± 18.69 | 79.4 ± 14.81 | 34.1 ± 10.86 **^ |
| | SVCG (mg) | 361.7 ± 75.94 | 335.9 ± 54.90 | 321.0 ± 34.82 | 210.8 ± 56.27 **^ | 71.8 ± 16.77 **^ |
| | LABC muscles (mg) | 537.7 ± 90.89 | 500.5 ± 80.02 | 485.2 ± 69.83 | 416.0 ± 53.61 **^ | 275.2 ± 25.42 **^ |
| | Glans penis (mg) | 81.7 ± 8.86 | 75.9 ± 6.08 | 73.7 ± 5.55 | 69.8 ± 7.25 **^ | 58.5 ± 5.12 **^ |
| | Cowper's glands (mg) | 28.0 ± 6.21 | 26.8 ± 3.06 | 21.1 ± 5.65 ** | 20.1 ± 2.39 ** | 11.2 ± 1.94 **^ |
| 13 | Starting Body Wt (g) | 273.4 ± 10.42 | 273.6 ± 10.41 | 273.3 ± 10.78 | 274.8 ± 10.48 | 273.3 ± 11.13 |
| | Terminal Body Wt (g) | 338.4 ± 17.57 | 344.7 ± 12.17 | 340.3 ± 16.34 | 347.4 ± 18.84 | 334.0 ± 13.12 |
| | Ventral prostate (mg) | 136.6 ± 33.74 | 118.8 ± 13.20 | 91.3 ± 22.93 **^ | 60.7 ± 8.20 **^ | 36.4 ± 9.93 **^ |
| | SVCG (mg) | 393.5 ± 51.83 | 358.5 ± 47.52 | 248.7 ± 45.50 **^ | 174.5 ± 31.98 **^ | 60.7 ± 13.00 **^ |
| | LABC muscles (mg) | 533.9 ± 25.92 | 511.5 ± 25.01 | 441.9 ± 33.29 **^ | 381.8 ± 50.41 **^ | 257.8 ± 51.50 **^ |
| | Glans penis (mg) | 91.1 ± 5.70 | 88.9 ± 4.42 | 79.8 ± 4.48 **^ | 76.8 ± 4.37 **^ | 64.0 ± 2.90 **^ |
| | Cowper's glands (mg) | 32.7 ± 5.98 | 32.7 ± 5.1 | 24.3 ± 6.53 **^ | 20.2 ± 3.07 **^ | 12.4 ± 2.51 **^ |
| 14 | Starting Body Wt (g) | 257.8 ± 7.79 | 257.7 ± 4.50 | 256.1 ± 6.72 | 258.2 ± 7.25 | 258.7 ± 4.60 |
| | Terminal Body Wt (g) | 340.6 ± 12.23 | 337.0 ± 8.56 | 338.8 ± 5.18 | 333.5 ± 9.43 | 335.3 ± 8.76 |
| | Ventral prostate (mg) ^b | 183.6 ± 21.96 | 149.7 ± 16.28 ** | 136.7 ± 14.60 **^ | 98.2 ± 10.79 **^ | 51.0 ± 10.33 **^ |
| | SVCG (mg) | 420.8 ± 92.86 | 458.7 ± 102.65 | 344.3 ± 46.63 | 247.7 ± 69.88 **^ | 96.4 ± 16.13 **^ |
| | LABC muscles (mg) | 590.4 ± 52.57 | 608.8 ± 95.73 | 529.3 ± 52.23 | 430.7 ± 32.79 **^ | 308.6 ± 31.24 **^ |
| | Glans penis (mg) | 76.4 ± 7.60 | 78.0 ± 11.24 | 77.7 ± 4.42 | 70.2 ± 5.66 * | 52.7 ± 2.56 **^ |
| | Cowper's glands (mg) ^b | 38.6 ± 4.22 | 36.0 ± 7.4 | 32.9 ± 5.13 | 25.9 ± 5.57 **^ | 16.2 ± 5.65 **^ |

R-square (%)

Overall means and [CV] for tissues at a given dose

| | OVR | TRT | LAB | | | | | |
|-----------------------|-----|-----|-----|----------|-------------|---------------|--------------|--------------|
| Ventral prostate (mg) | 81 | 60 | 16 | 131 [34] | 120 [21] ** | 104 [25] ** | 78 [21] **^ | 69 [34] **^ |
| SVCG (mg) | 91 | 64 | 19 | 348 [29] | 344 [30] | 271 [30] **^ | 187 [36] **^ | 69 [34] **^ |
| LABC (mg) | 83 | 50 | 34 | 506 [21] | 485 [25] | 445 [20] **^# | 374 [20] **^ | 256 [23] **^ |
| Glans penis (mg) | 75 | 53 | 23 | 80 [13] | 78 [12] | 75 [9] * | 70 [10] **^ | 57 [12] **^ |
| Cowper's glands (mg) | 78 | 51 | 26 | 30 [27] | 29 [26] | 25 [30] **^# | 20 [25] **^ | 12 [38] **^ |

SCVG – seminal vesicles and coagulating glands; OVR – Overall effect on tissue; TRT - Effect of treatments; LAB - Effect of laboratory; CV - Coefficient of variation.

*, ** Significantly different from control at P<0.05 and P<0.01, respectively, using T-test pairwise comparisons.

^ Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with either starting or terminal body weight adjustment.

Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with terminal body weight adjustment only.

^a The starting body weight from on the first day of substance administration and the terminal body weight is at necropsy approximately 24-hours after the last administration.

^b The VP and COWS were fixed and then weighed in laboratory 16

Suppl Material Table 3B. Vinclozolin (VIN) body weights, mandatory tissue weights and pooled statistics - stage 2, 0.4 mg TP/kg-bw/d (mean ± SD).

| Lab | Testosterone Propionate (mg/kg-bw/d) | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 |
|-----|--------------------------------------|----------------|-----------------------------|----------------|---------------------------------|--------------------------------|
| | Vinclozolin (mg/kg-bw/d) | 0 | 3 | 10 | 30 | 100 |
| 1 | Starting Body Wt (g) ^a | 205.2 ± 11.42 | 212.6 ± 11.97 | 209.6 ± 11.11 | 208.9 ± 14.78 | 206.4 ± 12.95 |
| | Terminal Body Wt (g) ^a | 219.9 ± 11.37 | 226.9 ± 14.96 | 223.4 ± 16.59 | 221.0 ± 14.55 | 219.0 ± 12.18 |
| | Ventral prostate (mg) | 106.5 ± 19.82 | 103.7 ± 25.01 | 94.5 ± 12.57 | 79.0 ± 16.38 * | 32.2 ± 8.04 *** [^] |
| | SVCG (mg) | 216.7 ± 58.54 | 261.7 ± 100.28 | 201.7 ± 39.71 | 143.3 ± 43.20 * | 45.0 ± 10.49 *** [^] |
| | LABC muscles (mg) | 310.0 ± 22.80 | 336.7 ± 56.45 | 295.0 ± 42.78 | 235.0 ± 31.46 *** [^] | 160.0 ± 14.14 *** [^] |
| | Glans penis (mg) | 66.0 ± 4.29 | 66.0 ± 4.98 | 58.3 ± 6.02 | 55.3 ± 7.06 *** [^] | 42.8 ± 5.49 *** [^] |
| | Cowper's glands (mg) | 21.7 ± 1.97 | 25.2 ± 7.19 | 18.7 ± 3.93 | 15.0 ± 2.19 *** [^] | 10.7 ± 2.58 *** [^] |
| 3 | Starting Body Wt (g) | 249.6 ± 15.42 | 245.6 ± 15.95 | 244.2 ± 13.94 | 241.5 ± 16.72 | 244.1 ± 14.68 |
| | Terminal Body Wt (g) | 309.0 ± 17.55 | 287.7 ± 25.08 | 299.8 ± 16.81 | 294.7 ± 16.73 | 297.9 ± 18.83 |
| | Ventral prostate (mg) | 179.4 ± 25.28 | 182.7 ± 55.77 | 172.2 ± 37.86 | 130.3 ± 22.47 * | 83.2 ± 26.24 *** [^] |
| | SVCG (mg) | 814.4 ± 130.88 | 913.8 ± 151.31 | 764.3 ± 98.40 | 532.9 ± 117.17 * [^] | 347.5 ± 49.45 *** [^] |
| | LABC muscles (mg) | 653.4 ± 81.23 | 699.5 ± 80.61 | 633.8 ± 57.25 | 483.3 ± 23.62 *** [^] | 369.3 ± 23.73 *** [^] |
| | Glans penis (mg) | 90.7 ± 7.83 | 89.5 ± 11.60 | 84.2 ± 3.08 | 91.8 ± 11.31 | 73.8 ± 6.94 *** [^] |
| | Cowper's glands (mg) | 31.7 ± 4.36 | 36.4 ± 7.65 | 33.4 ± 4.04 | 29.8 ± 2.43 | 20.7 ± 2.88 *** [^] |
| 5 | Starting Body Wt (g) | 234.2 ± 9.56 | 238.7 ± 15.90 | 234.7 ± 12.50 | 230.8 ± 13.04 | 234.0 ± 15.49 |
| | Terminal Body Wt (g) | 290.3 ± 15.06 | 293.3 ± 18.57 | 291.2 ± 16.74 | 281.2 ± 12.64 | 281.2 ± 21.20 |
| | Ventral prostate (mg) | 131.8 ± 35.65 | 123.7 ± 52.05 | 126.3 ± 35.30 | 110.2 ± 19.75 | 50.3 ± 9.87 *** [^] |
| | SVCG (mg) | 546.8 ± 106.80 | 463.9 ± 55.52 | 491.0 ± 79.51 | 341.3 ± 109.94 *** [^] | 146.5 ± 29.32 *** [^] |
| | LABC muscles (mg) | 467.0 ± 53.65 | 396.4 ± 45.83 ^{##} | 429.5 ± 60.06 | 352.3 ± 59.31 *** [^] | 256.7 ± 29.00 *** [^] |
| | Glans penis (mg) ^b | 89.5 ± 13.58 | 86.9 ± 8.46 | 87.1 ± 7.72 | 86.5 ± 7.96 (5) | 75.1 ± 6.69 (2) |
| | Cowper's glands (mg) | 34.3 ± 8.62 | 27.2 ± 5.64 | 32.9 ± 7.01 | 25.7 ± 3.83 | 16.4 ± 5.37 *** [^] |
| 7 | Starting Body Wt (g) | 253.7 ± 5.04 | 261.1 ± 15.25 | 259.1 ± 11.96 | 251.9 ± 7.37 | 257.4 ± 7.09 |
| | Terminal Body Wt (g) | 326.1 ± 11.41 | 337.3 ± 24.42 | 343.1 ± 17.71 | 328.6 ± 14.28 | 330.1 ± 9.03 |
| | Ventral prostate (mg) | 161.1 ± 28.20 | 131.4 ± 31.05 | 130.6 ± 23.82 | 92.9 ± 18.57 *** [^] | 50.7 ± 23.49 *** [^] |
| | SVCG (mg) | 420.3 ± 81.32 | 433.7 ± 49.81 | 397.7 ± 121.51 | 280.5 ± 55.20 *** [^] | 135.2 ± 47.47 *** [^] |
| | LABC muscles (mg) | 548.4 ± 68.92 | 501.3 ± 61.75 | 511.8 ± 94.43 | 376.8 ± 24.11 *** [^] | 282.4 ± 40.42 *** [^] |
| | Glans penis (mg) | 91.3 ± 6.57 | 91.6 ± 13.75 | 94.3 ± 10.24 | 86.7 ± 7.63 | 74.2 ± 11.33 *** [^] |
| | Cowper's glands (mg) | 36.7 ± 3.80 | 36.2 ± 2.77 | 34.7 ± 8.76 | 42.2 ± 33.77 | 18.2 ± 4.91 *** [^] |

R-square (%)

| | R-square (%) | | | Overall means and [CV] for tissues at a given dose | | | | | |
|-----------------------|--------------|-----|-----|--|----------|----------|-------------|-------------|--|
| | OVR | TRT | LAB | | | | | | |
| Ventral prostate (mg) | 71 | 57 | 18 | 145 [27] | 135 [37] | 131 [30] | 103 [26] ** | 54 [47] ** | |
| SVCG (mg) | 81 | 40 | 48 | 487 [49] | 518 [51] | 464 [48] | 325 [51] ** | 169 [70] ** | |
| LABC (mg) | 76 | 37 | 50 | 495 [28] | 471 [33] | 468 [30] | 361 [27] ** | 267 [30] ** | |
| Glans penis (mg) | 43 | 16 | 62 | 84 [16] | 84 [17] | 81 [19] | 80 [21] | 65 [26] ** | |
| Cowper's glands (mg) | 63 | 37 | 32 | 31 [25] | 31 [25] | 30 [30] | 28 [67] ** | 17 [33] ** | |

SCVG – seminal vesicles and coagulating glands; OVR – Overall effect on tissue; TRT - Effect of treatments; LAB - Effect of laboratory; CV - Coefficient of variation.

*, ** Significantly different from control at P<0.05 and P<0.01, respectively, using T-test pairwise comparisons.

[^] Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with either starting or terminal body weight adjustment.

^{##} Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with starting body weight adjustment only.

^a The starting body weight is from the first day of substance administration and the terminal body weight is at necropsy approximately 24-hours after the last administration.

^b If preputial separation was incomplete, the GP was not dissected and weighed. If the group size was decreased as a result, actual numbers per group are in parenthesis.

Suppl Material Table 4A. *p,p'*-DDE (DDE) body weights, mandatory tissue weights and pooled statistics - stage-1, 0.2 mg TP/kg-bw/d (mean ± SD).

| Lab | Testosterone Propionate (mg/kg-bw/d) | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 |
|-----|--------------------------------------|---------------|------------------|---------------|-------------------|-------------------|
| | <i>p,p'</i> -DDE (mg/kg-bw/d) | 0 | 3 | 10 | 30 | 100 |
| 10 | Starting Body Wt (g) ^a | 220.8 ± 8.33 | 219.8 ± 8.72 | 219.9 ± 7.31 | 220.5 ± 8.99 | 224.8 ± 6.10 |
| | Terminal Body Wt (g) ^a | 276.6 ± 11.71 | 270.2 ± 9.94 | 272.6 ± 8.38 | 274.7 ± 11.41 | 273.0 ± 8.01 |
| | Ventral prostate (mg) | 106.2 ± 13.20 | 89.8 ± 6.28 ** | 100.0 ± 18.09 | 71.7 ± 13.49 **^ | 52.4 ± 8.47 **^ |
| | SVCG (mg) | 225.7 ± 49.00 | 219.4 ± 29.11 | 202.4 ± 13.19 | 164.5 ± 35.71 **^ | 75.1 ± 11.69 **^ |
| | LABC muscles (mg) | 300.3 ± 31.26 | 305.7 ± 22.67 | 290.3 ± 33.57 | 309.0 ± 59.86 | 209.9 ± 16.29 **^ |
| | Glans penis (mg) | 67.0 ± 4.45 | 62.3 ± 5.13 | 66.3 ± 3.02 | 65.0 ± 5.42 | 56.6 ± 7.47 **^ |
| | Cowper's glands (mg) | 21.0 ± 2.35 | 21.5 ± 3.1 | 19.8 ± 1.28 | 15.4 ± 2.93 **^ | 11.0 ± 2.18 **^ |
| 11 | Starting Body Wt (g) | 237.6 ± 7.92 | 237.1 ± 8.75 | 237.9 ± 9.29 | 238.9 ± 9.06 | 237.3 ± 9.78 |
| | Terminal Body Wt (g) | 313.4 ± 16.57 | 313.4 ± 11.52 | 313.0 ± 12.67 | 317.3 ± 14.54 | 303.3 ± 17.14 |
| | Ventral prostate (mg) | 137.8 ± 33.84 | 125.7 ± 26.44 | 128.8 ± 22.07 | 93.6 ± 26.49 ** | 51.1 ± 16.36 **^ |
| | SVCG (mg) | 387.2 ± 63.24 | 272.3 ± 21.77 ** | 377.0 ± 47.69 | 256.0 ± 68.18 **^ | 88.3 ± 42.45 **^ |
| | LABC muscles (mg) | 549.9 ± 35.88 | 521.9 ± 63.63 | 519.4 ± 57.96 | 458.5 ± 59.68 **^ | 300.4 ± 31.12 **^ |
| | Glans penis (mg) | 73.3 ± 2.72 | 76.5 ± 3.90 | 73.5 ± 2.72 | 73.6 ± 3.46 | 63.0 ± 3.04 **^ |
| | Cowper's glands (mg) | 27.2 ± 7.21 | 21.8 ± 4.43 | 28.3 ± 4.77 | 23.7 ± 7.17 | 17.4 ± 3.96 **^ |
| 12 | Starting Body Wt (g) | 170.9 ± 6.87 | 171.4 ± 3.47 | 171.1 ± 5.77 | 170.5 ± 4.25 | 172.0 ± 4.98 |
| | Terminal Body Wt (g) | 240.9 ± 7.31 | 241.4 ± 6.78 | 241.4 ± 9.46 | 238.0 ± 6.45 | 235.8 ± 8.61 |
| | Ventral prostate (mg) | 90.6 ± 16.56 | 79.1 ± 7.84 | 88.1 ± 14.65 | 89.6 ± 12.10 | 56.5 ± 7.03 **^ |
| | SVCG (mg) | 282.8 ± 33.32 | 246.2 ± 48.56 | 240.0 ± 27.39 | 231.6 ± 39.18 ** | 152.0 ± 31.77 **^ |
| | LABC muscles (mg) | 435.7 ± 74.78 | 430.3 ± 52.45 | 407.0 ± 14.95 | 408.2 ± 55.67 | 311.9 ± 28.81 **^ |
| | Glans penis (mg) | 65.5 ± 8.62 | 64.9 ± 3.66 | 63.8 ± 5.80 | 66.9 ± 6.69 | 52.0 ± 10.93 **^ |
| | Cowper's glands (mg) | 26.2 ± 4.04 | 26.7 ± 4.9 | 25.4 ± 2.77 | 25.9 ± 3.46 | 17.0 ± 2.17 **^ |
| 14 | Starting Body Wt (g) | 244.3 ± 6.97 | 243.2 ± 7.46 | 242.6 ± 4.73 | 244.9 ± 5.38 | 245.1 ± 6.86 |
| | Terminal Body Wt (g) | 319.4 ± 14.69 | 326.9 ± 10.90 | 322.9 ± 6.93 | 323.6 ± 7.73 | 307.3 ± 12.49 |
| | Ventral prostate (mg) | 153.3 ± 20.50 | 158.4 ± 40.49 | 165.9 ± 43.29 | 141.8 ± 16.57 | 77.6 ± 27.64 **^ |
| | SVCG (mg) | 371.1 ± 56.95 | 432.6 ± 47.60 | 411.8 ± 60.35 | 326.1 ± 81.75 | 148.1 ± 47.07 **^ |
| | LABC muscles (mg) | 518.7 ± 11.70 | 574.3 ± 39.93 ** | 547.0 ± 38.67 | 490.9 ± 54.06 | 291.3 ± 31.25 **^ |
| | Glans penis (mg) | 77.3 ± 3.89 | 75.9 ± 4.87 | 76.5 ± 5.63 | 74.0 ± 4.29 | 60.8 ± 2.10 **^ |
| | Cowper's glands (mg) | 33.9 ± 6.42 | 33.8 ± 5.6 | 32.8 ± 4.31 | 32.6 ± 9.05 | 20.2 ± 5.79 **^ |
| 16 | Starting Body Wt (g) | 224.6 ± 10.24 | 223.8 ± 9.60 | 223.6 ± 12.35 | 222.5 ± 9.98 | 224.0 ± 9.93 |
| | Terminal Body Wt (g) | 292.7 ± 23.38 | 291.0 ± 15.15 | 290.4 ± 18.64 | 293.2 ± 15.55 | 289.4 ± 12.62 |
| | Ventral prostate (mg) ^b | 115.0 ± 18.8 | 101.3 ± 27.6 | 103.3 ± 16.5 | 74.7 ± 18.3 **^ | 48.7 ± 12.2 **^ |
| | SVCG (mg) | 237.2 ± 27.21 | 219.5 ± 41.02 | 251.4 ± 48.84 | 156.8 ± 33.24 **^ | 82.7 ± 23.07 **^ |
| | LABC muscles (mg) | 495.5 ± 79.30 | 496.6 ± 30.97 | 450.9 ± 48.10 | 395.1 ± 30.79 **^ | 301.5 ± 42.63 **^ |
| | Glans penis (mg) | 81.0 ± 6.76 | 80.1 ± 3.27 | 77.6 ± 4.85 | 76.2 ± 5.02 | 66.7 ± 6.76 **^ |
| | Cowper's glands (mg) ^b | 30.2 ± 4.55 | 28.1 ± 5.1 | 25.5 ± 4.43 | 24.2 ± 6.02 ** | 12.3 ± 3.13 **^ |

Suppl Material Table 4A continued. *p,p'*-DDE (DDE) body weights, mandatory tissue weights and pooled statistics - stage-1, 0.2 mg TP/kg-bw/d (mean ± SD).

| Lab | Testosterone Propionate (mg/kg-bw/d) | R-square (%) | | | Overall means and [CV] for tissues at a given dose | | | | |
|-----------------------|--------------------------------------|--------------|-----|-----|--|-------------|-----------|--------------|--------------|
| | <i>p,p'</i> -DDE (mg/kg-bw/d) | OVR | TRT | LAB | 0.2 0 | 0.2 3 | 0.2 10 | 0.2 30 | 0.2 100 |
| Ventral prostate (mg) | | 63 | 36 | 32 | 121 [25] | 111 [34] | 117 [31] | 94 [33] **^ | 57 [32] **^ |
| SVCG (mg) | | 45 | 45 | 31 | 301 [27] | 278 [32] ** | 297 [31] | 227 [36] **^ | 109 [42] **^ |
| LABC (mg) | | 69 | 37 | 42 | 460 [22] | 466 [22] | 443 [23] | 412 [19] **^ | 283 [17] **^ |
| Glans penis (mg) | | 54 | 30 | 37 | 73 [11] | 72 [11] | 72 [10] | 71 [9] | 60 [14] **^ |
| Cowper's glands (mg) | | 56 | 33 | 29 | 28 [24] | 26 [24] | 26 [21] | 24 [33] ** | 16 [31] **^ |

SCVG – seminal vesicles and coagulating glands; OVR – Overall effect on tissue; TRT - Effect of treatments; LAB - Effect of laboratory; CV - Coefficient of variation.

*,** Significantly different from control at P<0.05 and P<0.01, respectively, using T-test pairwise comparisons.

^ Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with either starting or terminal body weight adjustment.

^a The starting body weight is from the first day of substance administration and the terminal body weight is at necropsy approximately 24-hours after the last administration.

^b The VP and COWS were fixed and then weighed in laboratory 16.

Suppl Material Table 4B. *p,p'*-DDE (DDE) body weights, mandatory tissue weights and pooled statistics - stage-2, 0.4 mg TP/kg-bw/d (mean ± SD).

| Lab | Testosterone Propionate (mg/kg-bw/d) | 0.4 | | 0.4 | | 0.4 | | 0.4 | |
|-----|--------------------------------------|----------------|----------------|----------------|-------------------------------|--------------------------------|--|-----|--|
| | <i>p,p'</i> -DDE (mg/kg-bw/d) | 0 | 5 | 16 | 50 | 160 | | | |
| 3 | Starting Body Wt (g) ^a | 202.6 ± 13.22 | 205.2 ± 18.74 | 210.7 ± 16.70 | 205.6 ± 13.89 | 209.2 ± 12.48 | | | |
| | Terminal Body Wt (g) ^a | 259.3 ± 20.92 | 261.1 ± 34.32 | 273.5 ± 20.22 | 257.1 ± 21.56 | 228.5 ± 32.18 | | | |
| | Ventral prostate (mg) | 152.7 ± 16.11 | 156.1 ± 32.23 | 147.2 ± 19.51 | 94.3 ± 21.81 * | 40.1 ± 22.69 ** [^] | | | |
| | SVCG (mg) | 539.4 ± 77.45 | 601.4 ± 133.48 | 523.8 ± 85.71 | 401.9 ± 97.74 | 127.9 ± 54.21 ** [^] | | | |
| | LABC muscles (mg) | 528.8 ± 83.97 | 498.4 ± 75.97 | 451.3 ± 27.73 | 369.9 ± 40.58 ** [^] | 194.2 ± 36.01 ** [^] | | | |
| | Glans penis (mg) | 80.2 ± 10.13 | 80.9 ± 9.92 | 76.4 ± 6.14 | 73.6 ± 7.84 | 53.8 ± 8.18 ** [^] | | | |
| | Cowper's glands (mg) | 29.3 ± 5.06 | 27.4 ± 1.68 | 23.5 ± 4.3 | 17.3 ± 2.54 ** [^] | 10.7 ± 2.89 ** [^] | | | |
| 4 | Starting Body Wt (g) | 278.2 ± 12.07 | 278.0 ± 11.75 | 280.2 ± 19.85 | 278.2 ± 13.56 | 279.0 ± 15.56 | | | |
| | Terminal Body Wt (g) | 377.9 ± 19.85 | 364.4 ± 11.71 | 376.6 ± 38.44 | 356.8 ± 23.13 | 333.7 ± 28.80* | | | |
| | Ventral prostate (mg) | 183.8 ± 81.46 | 166.1 ± 22.94 | 202.0 ± 48.74 | 159.3 ± 34.67 | 90.9 ± 27.43 ** [^] | | | |
| | SVCG (mg) | 551.2 ± 179.45 | 599.5 ± 185.33 | 594.2 ± 121.37 | 483.8 ± 194.37 | 310.0 ± 109.74 ** | | | |
| | LABC muscles (mg) | 635.2 ± 72.45 | 616.5 ± 72.95 | 619.1 ± 47.67 | 525.5 ± 57.59 ** | 338.5 ± 43.53 ** [^] | | | |
| | Glans penis (mg) | 101.4 ± 6.34 | 100.9 ± 17.35 | 107.1 ± 7.16 | 100.2 ± 13.81 | 83.8 ± 13.63 * | | | |
| | Cowper's glands (mg) | 45.3 ± 6.66 | 45.7 ± 5.80 | 42.8 ± 5.41 | 33.2 ± 8.24 ** [^] | 28.0 ± 5.98 ** [^] | | | |
| 8 | Starting Body Wt (g) | 248.7 ± 12.81 | 247.7 ± 12.20 | 248.5 ± 13.68 | 248.3 ± 12.28 | 248.6 ± 14.56 | | | |
| | Terminal Body Wt (g) | 325.1 ± 19.36 | 325.9 ± 13.00 | 321.0 ± 17.19 | 322.1 ± 20.40 | 299.3 ± 24.69* | | | |
| | Ventral prostate (mg) | 210.4 ± 22.59 | 200.4 ± 24.02 | 195.9 ± 25.96 | 163.4 ± 25.67 * [^] | 78.0 ± 21.64 ** [^] | | | |
| | SVCG (mg) | 693.9 ± 78.29 | 590.2 ± 107.61 | 701.2 ± 131.03 | 460.8 ± 73.67 ** [^] | 214.5 ± 45.64 ** [^] | | | |
| | LABC muscles (mg) | 655.7 ± 80.55 | 579.8 ± 29.46 | 606.2 ± 54.61 | 509.8 ± 37.96 * [^] | 341.0 ± 108.73 ** [^] | | | |
| | Glans penis (mg) | 97.4 ± 8.18 | 84.5 ± 3.70 * | 92.7 ± 9.70 | 87.0 ± 6.20 | 68.4 ± 12.63 ** [^] | | | |
| | Cowper's glands (mg) | 50.8 ± 9.69 | 51.6 ± 10.14 | 46.1 ± 5.53 | 40.8 ± 9.59 * | 27.0 ± 4.53 ** [^] | | | |
| 9 | Starting Body Wt (g) | 244.2 ± 10.65 | 245.8 ± 11.58 | 245.3 ± 9.56 | 244.8 ± 11.03 | 244.0 ± 14.03 | | | |
| | Terminal Body Wt (g) | 335.3 ± 17.83 | 327.7 ± 15.53 | 326.8 ± 18.03 | 337.5 ± 15.41 | 317.8 ± 30.10 | | | |
| | Ventral prostate (mg) | 144.2 ± 23.18 | 123.6 ± 13.05 | 123.0 ± 37.41 | 105.4 ± 10.88 * | 71.4 ± 8.21 ** [^] | | | |
| | SVCG (mg) | 474.9 ± 37.42 | 423.8 ± 73.33 | 396.2 ± 78.63 | 382.8 ± 36.77 * [^] | 229.2 ± 26.02 ** [^] | | | |
| | LABC muscles (mg) | 372.0 ± 28.74 | 372.6 ± 43.20 | 340.4 ± 26.08 | 314.5 ± 29.16 ** [^] | 231.2 ± 34.65 ** [^] | | | |
| | Glans penis (mg) | 110.6 ± 4.53 | 111.0 ± 10.63 | 112.0 ± 9.57 | 105.7 ± 4.75 | 88.3 ± 7.40 ** [^] | | | |
| | Cowper's glands (mg) | 36.7 ± 2.91 | 33.8 ± 5.32 | 31.4 ± 7.17 | 29.4 ± 4.11 * | 19.1 ± 2.38 ** [^] | | | |

R-square (%)

| | R-square (%) | | | Overall means and [CV] for tissues at a given dose | | | | | |
|-----------------------|--------------|-----|-----|--|----------|-------------------------|--------------------------|--------------------------|--|
| | OVR | TRT | LAB | | | | | | |
| Ventral prostate (mg) | 68 | 54 | 15 | 173 [29] | 160 [25] | 162 [30] | 122 [38] ** [^] | 64 [46] ** [^] | |
| SVCG (mg) | 73 | 65 | 7.1 | 565 [24] | 545 [28] | 550 [27] | 394 [38] ** [^] | 193 [50] ** [^] | |
| LABC (mg) | 81 | 49 | 36 | 548 [24] | 506 [24] | 498 [27] * | 409 [31] ** [^] | 268 [36] ** [^] | |
| Glans penis (mg) | 56 | 27 | 18 | 97 [14] | 95 [18] | 95 [15] | 87 [15] * | 71 [22] ** [^] | |
| Cowper's glands (mg) | 70 | 37 | 48 | 41 [26] | 39 [31] | 35 [30] ** [^] | 28 [42] ** [^] | 19 [47] ** [^] | |

SCVG – seminal vesicles and coagulating glands; OVR – Overall effect on tissue; TRT - Effect of treatments; LAB - Effect of laboratory; CV - Coefficient of variation.

*, ** Significantly different from control at P<0.05 and P<0.01, respectively, using T-test pairwise comparisons.

[^] Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with either starting or terminal body weight adjustment.

Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with terminal body weight adjustment only.

Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with starting body weight adjustment only.

^a The starting body weight is from the first day of substance administration and the terminal body weight is at necropsy approximately 24-hours after the last administration.

Suppl Material Table 5. Procymidone (PRO) body weights, mandatory tissue weights and pooled statistics (mean ± SD).

| Lab | Testosterone Propionate (mg/kg-bw/d) | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 |
|-----------------|--------------------------------------|-------------------|-----------------|--------------------|---------------------|--------------------|
| | Procymidone (mg/kg-bw/d) | 0 | 3 | 10 | 30 | 100 |
| 2 | Starting Body Wt (g) ^a | 218.0 ± 13.59 | 218.7 ± 7.69 | 214.7 ± 11.74 | 222.7 ± 9.67 | 216.5 ± 14.24 |
| | Terminal Body Wt (g) ^a | 307.0 ± 17.57 | 305.4 ± 6.96 | 297.0 ± 16.21 | 301.1 ± 16.27 | 295.0 ± 16.97 |
| | Ventral prostate (mg) | 173.8 ± 32.53 | 180.2 ± 43.10 | 150.9 ± 52.33 * | 103.3 ± 16.49 ***^ | 52.7 ± 23.55 ***^ |
| | SVCG (mg) | 356.2 ± 53.09 | 362.1 ± 46.86 | 406.3 ± 176.22 | 215.6 ± 59.20 * | 145.7 ± 69.80 ***^ |
| | LABC muscles (mg) | 292.6 ± 41.88 | 339.7 ± 33.72 | 321.7 ± 79.39 | 277.9 ± 40.28 | 204.3 ± 31.79 ***^ |
| | Glans penis (mg) | 79.1 ± 4.94 | 83.2 ± 19.96 | 85.6 ± 7.75 | 79.7 ± 10.98 | 66.6 ± 18.60 |
| | Cowper's glands (mg) | 32.7 ± 8.00 | 30.4 ± 8.32 | 31.4 ± 8.92 | 29.1 ± 14.32 | 15.6 ± 4.96 ***^ |
| 7 | Starting Body Wt (g) | 248.4 ± 3.33 | 249.3 ± 8.05 | 234.1 ± 9.13 | 248.0 ± 11.67 | 246.2 ± 9.97 |
| | Terminal Body Wt (g) | 325.5 ± 20.55 | 322.8 ± 6.77 | 304.3 ± 20.97 | 317.0 ± 23.65 | 308.8 ± 12.23 |
| | Ventral prostate (mg) | 157.4 ± 18.02 | 140.5 ± 49.23 | 103.8 ± 33.01 | 80.4 ± 25.95 ***^ | 57.9 ± 19.68 ***^ |
| | SVCG (mg) | 485.3 ± 36.90 | 475.1 ± 105.59 | 396.6 ± 49.11 | 224.1 ± 48.65 ***^ | 205.8 ± 76.43 ***^ |
| | LABC muscles (mg) | 541.7 ± 62.63 | 514.5 ± 45.79 | 468.0 ± 118.45 | 324.6 ± 130.67 ***^ | 333.1 ± 62.28 ***^ |
| | Glans penis (mg) | 91.7 ± 15.20 | 96.9 ± 12.29 | 85.3 ± 4.43 | 78.5 ± 8.82 | 81.2 ± 7.56 |
| | Cowper's glands (mg) | 36.8 ± 10.21 | 34.6 ± 9.05 | 29.5 ± 9.32 | 22.3 ± 2.57 ***^ | 21.5 ± 6.36 ***^ |
| 8A ^b | Starting Body Wt (g) | 248.7 ± 12.81 (5) | 248.2 ± 8.95 | 248.0 ± 11.94 (4) | 247.8 ± 10.82 | 248.5 ± 13.24 (5) |
| | Terminal Body Wt (g) | 325.1 ± 19.36 | 319.1 ± 16.43 | 317.6 ± 7.60 | 314.8 ± 17.74 | 312.6 ± 15.87** |
| | Ventral prostate (mg) | 210.4 ± 22.59 | 206.8 ± 8.64 | 151.8 ± 31.83 ***^ | 124.3 ± 13.54 ***^ | 67.8 ± 10.92 ***^ |
| | SVCG (mg) | 693.9 ± 78.29 | 612.3 ± 95.93 | 479.7 ± 41.19 ***^ | 388.3 ± 64.40 ***^ | 212.6 ± 56.76 ***^ |
| | LABC muscles (mg) | 655.7 ± 80.55 | 589.4 ± 50.02 | 537.3 ± 52.33 ***^ | 441.6 ± 26.28 ***^ | 318.6 ± 38.01 ***^ |
| | Glans penis (mg) | 97.4 ± 8.18 | 88.0 ± 3.34 | 88.7 ± 8.81 | 78.9 ± 5.48 ***^ | 70.4 ± 11.87 ***^ |
| | Cowper's glands (mg) | 50.8 ± 9.69 | 49.7 ± 4.87 | 41.5 ± 12.39 | 41.3 ± 11.35 | 24.2 ± 4.63 ***^ |
| 8B ^b | Starting Body Wt (g) | 251.2 ± 6.49 | 251.2 ± 8.75 | 249.7 ± 8.68 | 248.3 ± 6.95 | 249.2 ± 6.55 |
| | Terminal Body Wt (g) | 333.2 ± 17.58 | 330.6 ± 17.91 | 329.1 ± 13.81 | 319.7 ± 11.30 | 310.9 ± 13.99** |
| | Ventral prostate (mg) | 214.2 ± 19.13 | 181.9 ± 37.40 | 140.2 ± 22.69 ***^ | 136.7 ± 19.89 ***^ | 68.7 ± 16.64 ***^ |
| | SVCG (mg) | 581.5 ± 125.60 | 580.1 ± 96.63 | 498.7 ± 76.13 | 404.2 ± 29.43 ***^ | 189.9 ± 53.51 ***^ |
| | LABC muscles (mg) | 654.1 ± 58.88 | 642.2 ± 48.05 | 571.3 ± 58.51 | 488.5 ± 42.11 ***^ | 319.1 ± 43.64 ***^ |
| | Glans penis (mg) | 86.8 ± 6.57 | 82.6 ± 11.94 | 79.1 ± 6.36 | 73.8 ± 7.69 ***^ | 60.7 ± 2.90 ***^ |
| | Cowper's glands (mg) | 45.6 ± 6.07 | 40.7 ± 5.9 | 34.6 ± 3.63 ***^ | 29.9 ± 4.32 ***^ | 19.4 ± 3.29 ***^ |
| 9 | Starting Body Wt (g) | 248.7 ± 12.68 | 248.0 ± 7.75 | 247.3 ± 8.98 | 248.3 ± 8.78 | 249.2 ± 7.88 |
| | Terminal Body Wt (g) | 338.0 ± 19.10 | 336.2 ± 14.77 | 335.3 ± 15.56 | 329.7 ± 8.80 | 331.5 ± 16.39 |
| | Ventral prostate (mg) | 145.8 ± 15.41 | 138.7 ± 18.71 | 118.9 ± 17.33 ***^ | 111.5 ± 16.78 ***^ | 76.4 ± 9.43 ***^ |
| | SVCG (mg) | 488.8 ± 51.60 | 445.7 ± 39.53 | 403.1 ± 30.92 ***^ | 282.1 ± 27.01 ***^ | 255.0 ± 21.14 ***^ |
| | LABC muscles (mg) | 393.6 ± 30.95 | 355.0 ± 30.28 * | 346.6 ± 29.13 ***^ | 275.0 ± 25.46 ***^ | 252.0 ± 18.15 ***^ |
| | Glans penis (mg) | 124.1 ± 13.12 | 115.4 ± 7.76 | 113.1 ± 7.08 * | 108.7 ± 6.45 ***^ | 107.9 ± 5.18 ***^ |
| | Cowper's glands (mg) | 40.1 ± 3.29 | 35.4 ± 2.55 * | 31.6 ± 2.22 ***^ | 26.1 ± 2.44 ***^ | 20.8 ± 1.93 ***^ |

Suppl Material Table 8 continued. Procymidone (PRO) body weights, mandatory tissue weights and pooled statistics .

| Lab | Testosterone Propionate (mg/kg-bw/d) | | 0.4 | | 0.4 | | 0.4 | | 0.4 | |
|-----------------------|--------------------------------------|-----|--|----------|----------|----------------|----------------|----------------|-----|--|
| | Procymidone (mg/k-bw/d) | | 0 | | 3 | | 10 | | 30 | |
| R-square (%) | | | Overall means and [CV] for tissues at a given dose | | | | | | | |
| | OVR | TRT | LAB | | | | | | | |
| Ventral prostate (mg) | 76 | 67 | 8 | 180 [19] | 170 [25] | 132 [28] **, ^ | 111 [24] **, ^ | 65 [28] **, ^ | | |
| SVCG (mg) | 78 | 61 | 14 | 521 [26] | 495 [24] | 434 [23] * | 303 [31] **, ^ | 202 [32] **, ^ | | |
| LABC (mg) | 67 | 33 | 41 | 508 [31] | 488 [27] | 441 [28] * | 362 [30] **, ^ | 285 [22] **, ^ | | |
| Glans penis (mg) | 37 | 16 | 47 | 96 [19] | 93 [18] | 91 [15] | 84 [18] **, ## | 77 [25] **, ^ | | |
| Cowper's glands (mg) | 63 | 49 | 13 | 41 [24] | 38 [24] | 33 [25] **, ^ | 30 [34] **, ^ | 20 [25] **, ^ | | |

SCVG – seminal vesicles and coagulating glands; OVR – Overall effect on tissue; TRT - Effect of treatments; LAB - Effect of laboratory; CV - Coefficient of variation.

*,** Significantly different from control at P<0.05 and P<0.01, respectively, using T-test pairwise comparisons.

^ Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with either starting or terminal body weight adjustment.

Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with starting body weight adjustment only.

^a The starting body weight is from the first day of substance administration and the terminal body weight is at necropsy approximately 24-hours after the last administration.

^b Laboratory 8 performed two studies due to gavage errors reducing several; group sizes in study A (see n in parenthesis, starting body weights)

Suppl Material Table 6. Linuron (LIN) body weights, mandatory tissue weights and pooled statistics (mean ± SD).

| Lab | Testosterone Propionate (mg/kg-bw/d) | 0.4 | | | | |
|-----|--------------------------------------|----------------|----------------|---------------|-------------------|--------------------|
| | | 0 | 3 | 10 | 30 | 100 |
| 1 | Starting Body Wt (g) ^a | 205.2 ± 11.42 | 209.1 ± 9.41 | 209.6 ± 13.18 | 202.7 ± 9.69 | 206.5 ± 9.94 |
| | Terminal Body Wt (g) ^a | 219.9 ± 11.37 | 221.7 ± 17.58 | 218.9 ± 16.63 | 218.2 ± 11.13 | 203.1 ± 11.04* |
| | Ventral prostate (mg) | 106.5 ± 19.82 | 113.3 ± 16.66 | 122.5 ± 23.95 | 89.0 ± 20.10 | 60.7 ± 10.93 **^ |
| | SVCG (mg) | 216.7 ± 58.54 | 293.3 ± 54.28 | 265.0 ± 41.83 | 191.7 ± 35.45 * | 101.7 ± 11.69 **^ |
| | LABC muscles (mg) | 310.0 ± 22.80 | 368.3 ± 32.51 | 333.3 ± 49.67 | 286.7 ± 48.03 | 188.3 ± 44.46 **^ |
| | Glans penis (mg) | 66.0 ± 4.29 | 68.0 ± 8.53 | 65.8 ± 6.91 | 61.5 ± 5.89 | 55.2 ± 4.79 **^ |
| | Cowper's glands (mg) | 21.7 ± 1.97 | 30.2 ± 7.28 | 24.2 ± 2.14 | 23.3 ± 5.72 | 15.2 ± 1.47 **^ |
| 4 | Starting Body Wt (g) | 275.8 ± 11.58 | 279.2 ± 11.21 | 274.7 ± 12.19 | 276.2 ± 12.30 | 275.3 ± 12.08 |
| | Terminal Body Wt (g) | 372.3 ± 14.74 | 364.7 ± 15.59 | 355.7 ± 17.42 | 351.8 ± 14.84* | 330.9 ± 12.86** |
| | Ventral prostate (mg) | 167.1 ± 34.58 | 192.8 ± 35.16 | 203.2 ± 33.54 | 184.4 ± 38.47 | 99.0 ± 26.74 **^ |
| | SVCG (mg) | 484.6 ± 65.58 | 568.5 ± 172.20 | 536.1 ± 79.17 | 541.5 ± 103.25 | 293.4 ± 72.09 **^# |
| | LABC muscles (mg) | 651.3 ± 87.10 | 654.6 ± 93.90 | 631.1 ± 52.24 | 571.5 ± 54.51 | 438.0 ± 40.11 **^ |
| | Glans penis (mg) | 91.2 ± 5.90 | 94.4 ± 14.34 | 102.4 ± 11.32 | 101.1 ± 4.80 | 89.5 ± 16.77 |
| | Cowper's glands (mg) | 43.1 ± 7.41 | 37.8 ± 7.14 | 43.8 ± 6.61 | 40.5 ± 4.38 | 31.6 ± 5.68 **^ |
| 5 | Starting Body Wt (g) | 237.3 ± 15.37 | 245.3 ± 24.62 | 234.7 ± 19.24 | 238.5 ± 13.92 | 241.8 ± 14.20 |
| | Terminal Body Wt (g) | 281.2 ± 18.73 | 284.0 ± 22.71 | 280.0 ± 21.48 | 277.2 ± 18.17 | 264.2 ± 10.85 |
| | Ventral prostate (mg) | 114.2 ± 22.22 | 111.6 ± 14.95 | 111.6 ± 16.92 | 83.7 ± 21.10 * | 46.2 ± 11.28 **^ |
| | SVCG (mg) | 436.5 ± 97.17 | 388.6 ± 64.12 | 339.1 ± 71.55 | 247.9 ± 44.07 **^ | 140.6 ± 40.20 **^ |
| | LABC muscles (mg) | 377.5 ± 41.51 | 351.0 ± 7.38 | 349.5 ± 56.18 | 297.3 ± 23.22 **^ | 158.3 ± 33.15 **^ |
| | Glans penis (mg) ^b | 73.3 ± 6.81 | 75.0 ± 8.39 | 73.8 ± 6.60 | 79.0 ± 8.19 | 64.1 ± 3.98 (3) |
| | Cowper's glands (mg) | 24.9 ± 4.73 | 23.1 ± 4.04 | 24.6 ± 6.12 | 19.5 ± 4.04 | 12.2 ± 4.20 **^ |
| 6 | Starting Body Wt (g) | 231.4 ± 4.47 | 231.9 ± 8.09 | 228.5 ± 9.31 | 232.4 ± 10.65 | 228.9 ± 9.59 |
| | Terminal Body Wt (g) | 306.5 ± 9.96 | 310.5 ± 12.69 | 305.5 ± 8.63 | 302.3 ± 13.13 | 291.8 ± 17.62 |
| | Ventral prostate (mg) | 83.3 ± 33.97 | 109.5 ± 51.89 | 115.2 ± 25.07 | 109.8 ± 25.32 | 67.9 ± 18.94 |
| | SVCG (mg) | 371.7 ± 137.19 | 412.3 ± 92.28 | 394.7 ± 82.92 | 323.1 ± 44.27 | 255.6 ± 58.67 * |
| | LABC muscles (mg) | 477.7 ± 50.98 | 485.5 ± 59.16 | 492.3 ± 30.27 | 496.1 ± 42.24 | 427.7 ± 42.40 |
| | Glans penis (mg) | 95.7 ± 12.07 | 93.4 ± 11.77 | 85.1 ± 13.88 | 97.9 ± 4.91 | 92.7 ± 19.05 |
| | Cowper's glands (mg) | 24.1 ± 5.52 | 25.3 ± 2.93 | 24.6 ± 3.46 | 23.4 ± 5.54 | 24.6 ± 8.61 |

R-square (%)

OVR TRT LAB

Overall means and [CV] for tissues at a given dose

| | | | | | | | | |
|-----------------------|----|-----|----|----------|----------|----------|-------------|--------------|
| Ventral prostate (mg) | 59 | 32 | 33 | 118 [35] | 132 [36] | 139 [33] | 117 [45] | 69 [47] **^ |
| SVCG (mg) | 65 | 35 | 49 | 377 [31] | 416 [34] | 383 [32] | 326 [45] * | 200 [47] **^ |
| LABC (mg) | 63 | 22 | 60 | 454 [31] | 465 [29] | 450 [30] | 413 [32] ** | 309 [44] **^ |
| Glans penis (mg) | 26 | 3.8 | 66 | 82 [18] | 83 [19] | 82 [21] | 85 [20] | 77 [28] * |
| Cowper's glands (mg) | 43 | 16 | 49 | 28 [35] | 29 [27] | 30 [33] | 27 [36] | 21 [44] **^ |

SCVG – seminal vesicles and coagulating glands; OVR – Overall effect on tissue; TRT - Effect of treatments; LAB - Effect of laboratory; CV - Coefficient of variation.

*, ** Significantly different from control at P<0.05 and P<0.01, respectively, using T-test pairwise comparisons.

^ Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with either starting or terminal body weight adjustment.

Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with terminal body weight adjustment only.

Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with starting body weight adjustment only.

^a The starting body weight is from the first day of substance administration and the terminal body weight is at necropsy approximately 24-hours after the last administration.

^b If preputial separation was incomplete, the GP was not dissected and weighed. If the group size was decreased as a result, actual numbers per group are in parenthesis.

Suppl Material Table 7. Finasteride (FIN) body weights, mandatory tissue weights and pooled statistics (mean ± SD).

| Lab | Testosterone Propionate (mg/kg-bw/d) | 0.4 | | | | |
|-----|--------------------------------------|----------------|------------------------------|------------------------------|-------------------------------|--------------------------------|
| | Finasteride (mg/kg-bw/d) | 0 | 0.2 | 1 | 5 | 25 |
| 2 | Starting Body Wt (g) ^a | 211.5 ± 9.09 | 212.2 ± 10.65 | 208.8 ± 4.26 | 209.3 ± 6.89 | 211.8 ± 6.43 |
| | Terminal Body Wt (g) ^a | 301.2 ± 20.90 | 287.9 ± 18.69 | 288.5 ± 12.64 | 283.9 ± 21.19 | 293.2 ± 6.79 |
| | Ventral prostate (mg) | 133.1 ± 36.20 | 115.5 ± 21.60 | 67.4 ± 27.29 ^{**^} | 54.0 ± 16.10 ^{**^} | 42.7 ± 12.53 ^{**^} |
| | SVCG (mg) | 316.2 ± 107.89 | 186.0 ± 49.63 | 89.1 ± 57.74 ^{**^} | 102.3 ± 39.28 ^{**^} | 62.8 ± 50.88 ^{**^} |
| | LABC muscles (mg) | 301.1 ± 36.40 | 286.1 ± 20.89 | 254.6 ± 11.60 [*] | 254.5 ± 19.09 [*] | 247.6 ± 46.75 ^{**^} |
| | Glans penis (mg) | 79.7 ± 6.44 | 72.7 ± 7.13 | 72.2 ± 8.96 | 69.7 ± 8.53 | 70.2 ± 16.11 |
| | Cowper's glands (mg) | 28.8 ± 8.72 | 24.4 ± 2.68 | 15.8 ± 10.24 [*] | 14.7 ± 4.71 [*] | 10.3 ± 4.69 ^{**^} |
| 5 | Starting Body Wt (g) | 221.7 ± 13.03 | 222.7 ± 11.06 | 227.5 ± 9.85 | 228.3 ± 14.54 | 226.3 ± 8.04 |
| | Terminal Body Wt (g) | 272.8 ± 21.48 | 273.5 ± 17.24 | 278.0 ± 22.53 | 276.0 ± 22.92 | 275.0 ± 15.10 |
| | Ventral prostate (mg) | 155.1 ± 25.55 | 62.2 ± 14.14 ^{**^} | 58.2 ± 16.80 ^{**^} | 49.4 ± 38.22 ^{**^} | 36.8 ± 19.67 ^{**^} |
| | SVCG (mg) | 576.1 ± 96.66 | 166.4 ± 30.55 ^{**^} | 137.9 ± 30.00 ^{**^} | 114.7 ± 19.79 ^{**^} | 97.9 ± 16.83 ^{**^} |
| | LABC muscles (mg) | 463.9 ± 50.41 | 317.1 ± 40.87 ^{**^} | 336.8 ± 55.83 ^{**^} | 303.5 ± 58.30 ^{**^} | 242.7 ± 35.32 ^{**^} |
| | Glans penis (mg) ^b | 84.4 ± 6.03 | 71.9 ± 4.83 ^{**} | 68.3 ± 4.92 ^{**^} | 70.9 ± 5.65 ^{** (4)} | 61.5 ± 5.82 ^{**^} (3) |
| | Cowper's glands (mg) | 34.8 ± 4.84 | 21.3 ± 3.40 ^{**^} | 18.4 ± 2.55 ^{**^} | 15.3 ± 3.03 ^{**^} | 8.5 ± 2.36 ^{**^} |
| 6 | Starting Body Wt (g) | 240.4 ± 11.52 | 242.2 ± 10.10 | 240.8 ± 10.88 | 241.0 ± 6.14 | 238.0 ± 8.34 |
| | Terminal Body Wt (g) | 311.9 ± 18.24 | 316.7 ± 12.13 | 317.3 ± 14.90 | 313.9 ± 10.83 | 314.3 ± 13.60 |
| | Ventral prostate (mg) | 116.9 ± 27.88 | 73.2 ± 15.81 | 57.4 ± 27.09 ^{**^} | 53.4 ± 14.30 ^{**^} | 29.8 ± 13.44 ^{**^} |
| | SVCG (mg) | 425.5 ± 54.25 | 192.7 ± 58.04 ^{**^} | 212.5 ± 48.29 ^{**^} | 132.1 ± 27.73 ^{**^} | 139.6 ± 56.40 ^{**^} |
| | LABC muscles (mg) | 512.1 ± 70.15 | 455.5 ± 55.74 | 542.1 ± 48.95 | 408.7 ± 53.47 ^{**^} | 473.3 ± 33.73 |
| | Glans penis (mg) | 97.4 ± 8.64 | 90.2 ± 8.95 | 100.9 ± 11.04 | 85.1 ± 3.71 ^{**} | 99.5 ± 3.71 |
| | Cowper's glands (mg) | 26.4 ± 4.54 | 22.5 ± 5.10 | 26.6 ± 7.22 | 16.2 ± 6.07 ^{**^} | 15.0 ± 4.05 ^{**^} |
| 9 | Starting Body Wt (g) | 249.7 ± 9.81 | 255.2 ± 10.70 | 251.2 ± 8.66 | 252.8 ± 6.27 | 254.3 ± 7.06 |
| | Terminal Body Wt (g) | 322.3 ± 13.08 | 333.5 ± 14.10 | 330.3 ± 11.38 | 338.2 ± 14.47 | 334.3 ± 13.44 |
| | Ventral prostate (mg) | 122.0 ± 25.06 | 79.0 ± 11.56 ^{**^} | 72.6 ± 11.29 ^{**^} | 58.8 ± 7.48 ^{**^} | 45.1 ± 8.50 ^{**^} |
| | SVCG (mg) | 428.9 ± 45.19 | 274.6 ± 54.49 ^{**^} | 222.7 ± 14.82 ^{**^} | 172.2 ± 28.02 ^{**^} | 140.3 ± 14.50 ^{**^} |
| | LABC muscles (mg) | 385.8 ± 37.60 | 362.9 ± 31.72 | 304.5 ± 24.86 ^{**^} | 301.2 ± 15.61 ^{**^} | 301.8 ± 23.52 ^{**^} |
| | Glans penis (mg) | 106.6 ± 16.62 | 92.5 ± 6.44 [*] | 90.9 ± 5.74 [*] | 84.8 ± 4.43 ^{**^} | 82.1 ± 6.39 ^{**^} |
| | Cowper's glands (mg) | 33.1 ± 4.32 | 31.2 ± 4.67 | 27.3 ± 3.94 | 20.5 ± 4.51 ^{**^} | 16.0 ± 3.47 ^{**^} |

R-square (%)

OVR TRT LAB

| | OVR | TRT | LAB | Overall means and [CV] for tissues at a given dose | | | | |
|-----------------------|-----|-----|-----|--|-------------|-------------|-------------|-------------|
| Ventral prostate (mg) | 71 | 61 | 3.5 | 132 [23] | 83 [31] ** | 64 [33] ** | 54 [37] ** | 39 [38] ** |
| SVCG (mg) | 82 | 61 | 15 | 437 [26] | 205 [30] ** | 166 [41] ** | 131 [30] ** | 110 [45] ** |
| LABC (mg) | 56 | 15 | 60 | 416 [23] | 355 [21] ** | 359 [33] ** | 318 [22] ** | 316 [32] ** |
| Glans penis (mg) | 44 | 12 | 49 | 92 [16] | 82 [14] ** | 83 [19] ** | 78 [12] ** | 81 [21] ** |
| Cowper's glands (mg) | 64 | 46 | 10 | 31 [21] | 25 [22] * | 22 [37] ** | 17 [30] ** | 12 [38] ** |

SCVG – seminal vesicles and coagulating glands; OVR – Overall effect on tissue; TRT - Effect of treatments; LAB - Effect of laboratory; CV - Coefficient of variation.

*, ** Significantly different from control at P<0.05 and P<0.01, respectively, using T-test pairwise comparisons.

[^] Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with either starting or terminal body weight adjustment.

[#] Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with terminal body weight adjustment only.

^{##} Significantly different from control at P<0.05 using two-tailed Dunnett's multiple comparisons of the tissue with starting body weight adjustment only.

^a The starting body weight is from the first day of substance administration and the terminal body weight is at necropsy approximately 24-hours after the last administration.

^b If preputial separation was incomplete, the GP was not dissected and weighed. If the group size was decreased as a result, actual numbers per group are in parenthesis.

Section II. EHP 9666: OECD Validation of Rat Hershberger Assay: Phase-2 Dose Response Studies

A set of detailed data tables for the three optional tissues including means, standard deviations and statistical significance, for each laboratory and each chemical dose group.

This section contains the following tables of detailed data for Phase-2 of the OECD Hershberger Validation Program.

Suppl. Material Table 8. Optional organ weights methyltestosterone (MT) studies – stage 2 (mean \pm SD).

Suppl. Material Table 9. Optional organ weights trenbolone (TREN) studies (mean \pm SD).

Suppl. Material Table 10. Optional organ weights vinclozolin (VIN) studies – stage 2 (mean \pm SD).

Suppl. Material Table 11. Optional organ weights *p,p'*-DDE (DDE) studies – stage 2 (mean \pm SD).

Suppl. Material Table 12. Optional organ weights procymidone (PRO) studies (mean \pm SD).

Suppl. Material Table 13. Optional organ weights linuron (LIN) studies (mean \pm SD).

Suppl. Material Table 14. Optional organ weights finasteride (FIN) studies (mean \pm SD).

Suppl. Material Table 8. Dose Response for Ventral Prostate in Phase-1B (mg, mean \pm SD)

Suppl. Material Table 9. Dose Response for Seminal Vesicles and Coagulating Glands in Phase-1B (mg, mean \pm SD)

Suppl. Material Table 10. Dose Response for Levator Ani and Bulbocavernosus Muscles in Phase-1B (mg, mean \pm SD)

Suppl. Material Table 8. Optional organ weights methyltestosterone (MT) studies – stage 2 (mean ± SD).

| Lab | Methyl Testosterone (mg/kg-bw/d) | 0 | 0.5 | 2 | 10 | 40 |
|-----|----------------------------------|-----------------|-----------------|-----------------|--------------------|--------------------|
| 2 | Terminal Body Wt (g) | 300.9 ± 22.51 | 306.9 ± 14.57 | 296.8 ± 13.38 | 303.6 ± 21.42 | 309.3 ± 11.41 |
| | Liver (g) | 11.6 ± 0.93 | 11.9 ± 1.09 | 11.7 ± 0.95 | 11.8 ± 0.66 | 13.1 ± 1.04 ** |
| | (relative to bw) | 3.86% | 3.88% | 3.94% | 3.89% | 4.24% |
| | Adrenals (mg) | 65.9 ± 11.98 | 61.3 ± 9.85 | 51.4 ± 7.49 ** | 62.1 ± 7.68 | 53.5 ± 7.18 ** |
| | (relative to bw) | 0.0219% | 0.0200% | 0.0173% | 0.0205% | 0.0173% |
| | Kidneys (mg) | 2062.9 ± 214.41 | 2127.2 ± 176.65 | 2071.1 ± 178.22 | 2126.6 ± 80.26 | 2194.1 ± 176.12 |
| | (relative to bw) | 0.6856% | 0.6931% | 0.6978% | 0.7005% | 0.7094% |
| 4 | Terminal Body Wt (g) | 321.7 ± 16.31 | 331.6 ± 19.72 | 334.0 ± 17.69 | 322.9 ± 15.57 | 323.3 ± 20.70 |
| | Liver (g) | 13.7 ± 0.85 | 14.4 ± 1.35 | 15.1 ± 1.14 | 14.3 ± 0.85 | 14.9 ± 0.67 * |
| | (relative to bw) | 4.26% | 4.34% | 4.52% | 4.43% | 4.61% |
| | Adrenals (mg) | 56.8 ± 5.91 | 56.2 ± 7.51 | 58.8 ± 6.03 | 51.7 ± 6.83 | 46.7 ± 6.60 * |
| | (relative to bw) | 0.0177% | 0.0169% | 0.0176% | 0.0160% | 0.0144% |
| | Kidneys (mg) | 2100.8 ± 76.57 | 2213.7 ± 265.21 | 2319.4 ± 213.40 | 2318.3 ± 168.06 * | 2385.4 ± 178.43 ** |
| | (relative to bw) | 0.6530% | 0.6676% | 0.6944% | 0.7180% | 0.7378% |
| 6 | Terminal Body Wt (g) | 291.2 ± 7.49 | 302.0 ± 11.25 | 298.0 ± 16.33 | 293.5 ± 23.06 | 290.7 ± 14.88 |
| | Liver (g) | 13.5 ± 1.06 | 14.7 ± 1.77 | 14.7 ± 2.20 | 14.5 ± 1.82 | 14.5 ± 1.40 |
| | (relative to bw) | 4.64% | 4.87% | 4.93% | 4.94% | 4.99% |
| | Adrenals (mg) | 55.6 ± 2.39 | 54.0 ± 8.89 | 59.9 ± 12.61 | 53.8 ± 2.91 | 46.3 ± 4.81 * |
| | (relative to bw) | 0.0191% | 0.0179% | 0.0201% | 0.0183% | 0.0159% |
| | Kidneys (mg) | 2326.1 ± 207.46 | 2434.4 ± 169.78 | 2461.5 ± 312.41 | 2542.2 ± 231.14 | 2566.5 ± 291.1 * |
| | (relative to bw) | 0.7988% | 0.8061% | 0.8260% | 0.8662% | 0.8829% |
| 8 | Terminal Body Wt (g) | 319.6 ± 10.64 | 320.1 ± 15.70 | 313.5 ± 15.06 | 324.0 ± 12.37 | 321.4 ± 12.37 |
| | Liver (g) | 12.9 ± 1.05 | 13.2 ± 1.10 | 12.6 ± 1.00 | 13.7 ± 0.39 | 14.1 ± 1.10 * |
| | (relative to bw) | 4.04% | 4.12% | 4.02% | 4.23% | 4.39% |
| | Adrenals (mg) | 50.6 ± 4.34 | 51.5 ± 5.14 | 49.5 ± 9.93 | 53.0 ± 11.81 | 47.2 ± 6.67 |
| | (relative to bw) | 0.0158% | 0.0161% | 0.0158% | 0.0164% | 0.0147% |
| | Kidneys (mg) | 2081.6 ± 134.82 | 2189.8 ± 182.60 | 2103.2 ± 138.34 | 2404.7 ± 203.79 ** | 2380.9 ± 103.28 ** |
| | (relative to bw) | 0.6513% | 0.6841% | 0.6709% | 0.7422% | 0.7408% |

*,** Significantly different from control at P<0.05 and P<0.01, respectively, using T-test pairwise comparisons.

Suppl. Material Table 9. Optional organ weights trenbolone (TREN) studies (mean ± SD).

| Lab | Trenbolone (mg/kg-bw/d) | 0 | 0.3 | 1.5 | 8 | 40 |
|-----|-------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| 1 | Terminal Body Wt (g) | 207.4 ± 12.71 | 211.2 ± 14.91 | 209.4 ± 8.65 | 198.6 ± 9.22 | 189.7 ± 10.42* |
| | Liver (g) | 6.5 ± 0.52 | 6.4 ± 0.52 | 6.6 ± 0.62 | 6.6 ± 0.35 | 6.8 ± 0.61 |
| | (relative to bw) | 3.13% | 3.03% | 3.15% | 3.32% | 3.58% |
| | Adrenals (mg) | 65.2 ± 7.31 | 66.2 ± 9.90 | 65.1 ± 7.97 | 64.3 ± 8.73 | 66.1 ± 8.04 |
| | (relative to bw) | 0.0314% | 0.0313% | 0.0311% | 0.0324% | 0.0348% |
| | Kidneys (mg) | 1624.1 ± 109.79 | 1679.7 ± 166.09 | 1662.6 ± 107.27 | 1625.5 ± 95.99 | 1600.3 ± 94.85 |
| | (relative to bw) | 0.7831% | 0.7953% | 0.7940% | 0.8185% | 0.8436% |
| 3 | Terminal Body Wt (g) | 238.8 ± 17.47 | 243.4 ± 10.87 | 247.6 ± 19.25 | 236.9 ± 12.20 | 224.3 ± 23.93 |
| | Liver (g) | 10.4 ± 0.95 | 10.3 ± 0.76 | 10.7 ± 1.34 | 10.6 ± 0.87 | 10.4 ± 2.26 |
| | (relative to bw) | 4.35% | 4.24% | 4.31% | 4.46% | 4.61% |
| | Adrenals (mg) | 56.0 ± 7.71 | 45.9 ± 6.83 | 48.1 ± 7.63 | 42.9 ± 7.14 | 45.0 ± 5.61 |
| | (relative to bw) | 0.0235% | 0.0189% | 0.0194% | 0.0181% | 0.0201% |
| | Kidneys (mg) | 1600.3 ± 188.99 | 1523.2 ± 111.96 | 1485.1 ± 116.91 | 1582.8 ± 60.08 | 1501.1 ± 235.58 |
| | (relative to bw) | 0.6701% | 0.6258% | 0.5998% | 0.6681% | 0.6692% |
| 7 | Terminal Body Wt (g) | 305.4 ± 20.86 | 327.3 ± 24.20 | 312.8 ± 11.86 | 303.6 ± 30.84 | 271.2 ± 16.02* |
| | Liver (g) | 14.6 ± 1.68 | 18.7 ± 3.66 | 17.5 ± 1.47 | 17.8 ± 3.29 | 16.0 ± 1.65 |
| | (relative to bw) | 4.78% | 5.71% | 5.59% | 5.86% | 5.90% |
| | Adrenals (mg) | 54.6 ± 6.56 | 54.3 ± 8.84 | 55.4 ± 7.74 | 53.1 ± 7.97 | 55.1 ± 9.37 |
| | (relative to bw) | 0.0179% | 0.0166% | 0.0177% | 0.0175% | 0.0203% |
| | Kidneys (mg) | 2652.2 ± 236.06 | 2822.8 ± 267.25 | 2677.3 ± 208.58 | 2828.5 ± 382.49 | 2502.5 ± 128.33 |
| | (relative to bw) | 0.8684% | 0.8625% | 0.8559% | 0.9317% | 0.9228% |

*,** Significantly different from control at P<0.05 and P<0.01, respectively, using T-test pairwise comparisons.

Suppl. Material Table 10. Optional organ weights vinclozolin (VIN) studies – stage 2 (mean ± SD)

| Lab | Testosterone Prop. (mg/kg-bw/d) | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 |
|-----|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| | Vinclozolin (mg/kg-bw/d) | 0 | 3 | 10 | 30 | 100 |
| 1 | Terminal Body Wt (g) | 219.9 ± 11.37 | 226.9 ± 14.96 | 223.4 ± 16.59 | 221.0 ± 14.55 | 219.0 ± 12.18 |
| | Liver (g) | 6.6 ± 0.29 | 6.7 ± 0.53 | 6.7 ± 0.77 | 6.7 ± 0.94 | 7.2 ± 0.48 ** |
| | (relative to bw) | 3.00% | 2.95% | 3.00% | 3.03% | 3.29% |
| | Adrenals (mg) | 69.3 ± 12.79 | 63.7 ± 9.33 | 65.0 ± 8.51 | 77.5 ± 17.81 | 95.0 ± 12.90 ** |
| | (relative to bw) | 0.0315% | 0.0281% | 0.0291% | 0.0351% | 0.0434% |
| | Kidneys (mg) | 1681.7 ± 75.74 | 1748.3 ± 116.86 | 1645.0 ± 67.45 | 1680.0 ± 233.84 | 1756.7 ± 122.58 |
| | (relative to bw) | 0.7648% | 0.7705% | 0.7363% | 0.7602% | 0.8021% |
| 3 | Terminal Body Wt (g) | 309.0 ± 17.55 | 283.8 ± 25.08 | 299.8 ± 16.81 | 294.7 ± 16.73 | 297.9 ± 18.83 |
| | Liver (g) | 13.2 ± 1.71 | 13.0 ± 1.98 | 13.0 ± 0.916 | 13.7 ± 0.901 ** | 14.0 ± 1.39 ** |
| | (relative to bw) | 4.27% | 4.58% | 4.33% | 4.66% | 4.69% |
| | Adrenals (mg) | 49.4 ± 5.93 | 53.8 ± 8.10 | 59.7 ± 7.78 ** | 62.7 ± 8.21 ** | 62.3 ± 13.85 ** |
| | (relative to bw) | 0.0160% | 0.0190% | 0.0199% | 0.0213% | 0.0209% |
| | Kidneys (mg) | 1895.9 ± 179.90 | 1898.0 ± 180.58 | 1855.6 ± 211.91 | 1888.3 ± 133.50 | 1856.0 ± 202.25 |
| | (relative to bw) | 0.6136% | 0.6688% | 0.6189% | 0.6408% | 0.6230% |
| 5 | Terminal Body Wt (g) | 290.3 ± 15.06 | 293.3 ± 18.57 | 291.2 ± 16.74 | 281.2 ± 12.64 | 281.2 ± 21.20 |
| | Liver (g) | 10.4 ± 1.10 | 10.5 ± 1.02 | 10.7 ± 1.10 | 11.1 ± 0.70 * | 12.1 ± 1.11 ** |
| | (relative to bw) | 3.58% | 3.58% | 3.67% | 3.95% | 4.30% |
| | Adrenals (mg) | 60.1 ± 6.50 | 63.9 ± 9.04 | 60.6 ± 8.88 | 69.0 ± 8.55 * | 86.8 ± 19.01 ** |
| | (relative to bw) | 0.0207% | 0.0218% | 0.0208% | 0.0245% | 0.0309% |
| | Kidneys (mg) | 1763.2 ± 84.13 | 1811.0 ± 117.23 | 1886.0 ± 144.75 | 1740.3 ± 79.55 | 1793.8 ± 125.04 |
| | (relative to bw) | 0.6074% | 0.6175% | 0.6477% | 0.6189% | 0.6379% |
| 7 | Terminal Body Wt (g) | 326.1 ± 11.41 | 337.3 ± 24.42 | 343.1 ± 17.71 | 328.6 ± 14.28 | 330.1 ± 9.03 |
| | Liver (g) | 15.9 ± 1.43 | 17.4 ± 0.93 | 17.9 ± 1.99 | 17.9 ± 1.69 ** | 18.2 ± 1.15 ** |
| | (relative to bw) | 4.88% | 5.16% | 5.22% | 5.45% | 5.51% |
| | Adrenals (mg) | 59.5 ± 6.92 | 56.8 ± 9.52 | 63.7 ± 11.01 | 63.5 ± 5.87 | 71.1 ± 7.51 * |
| | (relative to bw) | 0.0182% | 0.0168% | 0.0186% | 0.0193% | 0.0215% |
| | Kidneys (mg) | 2720.4 ± 166.57 | 2691.8 ± 270.86 | 2950.0 ± 262.69 | 2709.8 ± 199.39 | 2712.1 ± 222.35 |
| | (relative to bw) | 0.8342% | 0.7980% | 0.8598% | 0.8247% | 0.8216% |

*, ** Significantly different from control at P<0.05 and P<0.01, respectively, using T-test pairwise comparisons.

Suppl. Material Table 11. Optional organ weights *p,p'*-DDE (DDE) studies – stage 2 (mean ± SD).

| Lab | Testosterone Prop. (mg/kg-bw/d) | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 |
|-----|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| | <i>p,p'</i> -DDE (mg/kg-bw/d) | 0 | 5 | 16 | 50 | 160 |
| 3 | Terminal Body Wt (g) | 259.3 ± 20.92 | 261.1 ± 34.32 | 273.5 ± 20.22 | 257.1 ± 21.56 | 228.5 ± 32.18 |
| | Liver (g) | 12.2 ± 0.99 | 12.9 ± 2.31 | 15.5 ± 1.51 ** | 16.7 ± 2.26 ** | 18.0 ± 2.89 ** |
| | (relative to bw) | 4.71% | 4.95% | 5.67% | 6.51% | 7.86% |
| | Adrenals (mg) | 44.8 ± 7.27 | 43.2 ± 7.98 | 44.5 ± 3.89 | 45.6 ± 3.60 | 51.0 ± 8.4 ** |
| | (relative to bw) | 0.0173% | 0.0165% | 0.0163% | 0.0177% | 0.0223% |
| | Kidneys (mg) | 1736.2 ± 106.59 | 1756.0 ± 259.19 | 1781.4 ± 197.78 | 1781.4 ± 161.22 | 1679.0 ± 241.0 |
| | (relative to bw) | 0.6703% | 0.6725% | 0.6514% | 0.6929% | 0.7348% |
| 4 | Terminal Body Wt (g) | 377.9 ± 19.85 | 364.4 ± 11.71 | 376.6 ± 38.44 | 356.8 ± 23.13 | 333.7 ± 28.80* |
| | Liver (g) | 15.7 ± 1.18 | 15.5 ± 0.72 | 18.2 ± 2.56 ** | 19.6 ± 1.54 ** | 23.1 ± 2.44 ** |
| | (relative to bw) | 4.15% | 4.25% | 4.83% | 5.49% | 6.88% |
| | Adrenals (mg) | 57.2 ± 7.79 | 56.9 ± 8.91 | 56.1 ± 5.31 | 52.2 ± 5.29 | 59.3 ± 7.34 |
| | (relative to bw) | 0.0151% | 0.0156% | 0.0149% | 0.0146% | 0.0177% |
| | Kidneys (mg) | 2265.1 ± 163.56 | 2232.5 ± 80.55 | 2306.4 ± 230.42 | 2217.2 ± 167.79 | 2214.5 ± 261.35 |
| | (relative to bw) | 0.5994% | 0.6127% | 0.6124% | 0.6214% | 0.6597% |
| 8 | Terminal Body Wt (g) | 325.1 ± 19.36 | 325.9 ± 13.00 | 321.0 ± 17.19 | 322.1 ± 20.40 | 299.3 ± 24.69* |
| | Liver (g) | 13.9 ± 1.28 | 14.7 ± 0.76 | 16.0 ± 1.16 ** | 19.0 ± 0.74 ** | 20.6 ± 2.99 ** |
| | (relative to bw) | 4.28% | 4.51% | 4.98% | 5.90% | 6.88% |
| | Adrenals (mg) | 51.2 ± 6.41 | 59.0 ± 3.70 | 55.3 ± 5.84 | 50.5 ± 9.42 | 55.6 ± 10.99 |
| | (relative to bw) | 0.0157% | 0.0181% | 0.0172% | 0.0157% | 0.0186% |
| | Kidneys (mg) | 2198.4 ± 186.19 | 2174.7 ± 105.99 | 2142.4 ± 118.00 | 2236.5 ± 125.02 | 2112.7 ± 151.36 |
| | (relative to bw) | 0.6762% | 0.6673% | 0.6674% | 0.6943% | 0.7059% |
| 9 | Terminal Body Wt (g) | 335.3 ± 17.83 | 327.7 ± 15.53 | 326.8 ± 18.03 | 337.5 ± 15.41 | 317.8 ± 30.10 |
| | Liver (g) | 16.0 ± 1.60 | 17.2 ± 1.19 * | 18.6 ± 1.33 ** | 23.1 ± 1.26 ** | 25.7 ± 3.35 ** |
| | (relative to bw) | 4.77% | 5.25% | 5.69% | 6.84% | 8.09% |
| | Adrenals (mg) | 54.5 ± 7.56 | 57.9 ± 6.00 | 60.4 ± 4.45 | 65.2 ± 4.11 | 58.7 ± 6.28 |
| | (relative to bw) | 0.0163% | 0.0177% | 0.0185% | 0.0193% | 0.0185% |
| | Kidneys (mg) | 2349.0 ± 96.38 | 2392.4 ± 118.63 | 2443.5 ± 172.32 | 2560.1 ± 157.59 | 2506.4 ± 226.47 |
| | (relative to bw) | 0.7006% | 0.7301% | 0.7477% | 0.7585% | 0.7887% |

*, ** Significantly different from control at P<0.05 and P<0.01, respectively, using T-test pairwise comparisons.

Suppl. Material Table 12. Optional organ weights procymidone (PRO) studies (mean ± SD).

| Lab | Testosterone Prop. (mg/kg-bw/d) | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 |
|-----------------|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| | Procymidone (mg/kg-bw/d) | 0 | 3 | 10 | 30 | 100 |
| 2 | Terminal Body Wt (g) | 307.0 ± 17.57 | 305.4 ± 6.96 | 297.0 ± 16.21 | 301.1 ± 16.27 | 295.0 ± 16.97 |
| | Liver (g) | 13.4 ± 0.78 | 13.1 ± 0.75 | 12.5 ± 0.98 | 13.8 ± 1.60 | 13.9 ± 0.84 * |
| | (relative to bw) | 4.36% | 4.29% | 4.21% | 4.58% | 4.71% |
| | Adrenals (mg) | 54.0 ± 9.04 | 63.4 ± 14.12 | 61.9 ± 9.86 | 66.2 ± 6.26 * | 80.6 ± 13.53 ** |
| | (relative to bw) | 0.0176% | 0.0208% | 0.0208% | 0.0220% | 0.0273% |
| | Kidneys (mg) | 2226.6 ± 199.91 | 2165.5 ± 129.50 | 2138.6 ± 100.53 | 2165.2 ± 107.41 | 2082.7 ± 95.33 |
| | (relative to bw) | 0.725% | 0.709% | 0.720% | 0.719% | 0.706% |
| 7 | Terminal Body Wt (g) | 325.5 ± 20.55 | 322.8 ± 6.77 | 304.3 ± 20.97 | 317.0 ± 23.65 | 308.8 ± 12.23 |
| | Liver (g) | 16.3 ± 1.67 | 17.4 ± 1.87 | 17.9 ± 2.00 ** | 18.7 ± 2.57 ** | 20.2 ± 0.70 ** |
| | (relative to bw) | 5.01% | 5.39% | 5.88% | 5.90% | 6.54% |
| | Adrenals (mg) | 57.8 ± 5.32 | 57.7 ± 7.25 | 61.8 ± 7.78 | 66.3 ± 7.22 * | 64.9 ± 7.07 |
| | (relative to bw) | 0.0178% | 0.0179% | 0.0203% | 0.0209% | 0.0210% |
| | Kidneys (mg) | 2818.3 ± 170.89 | 2705.2 ± 136.19 | 2659.2 ± 142.98 | 2759.5 ± 263.11 | 2722.6 ± 232.62 |
| | (relative to bw) | 0.866% | 0.838% | 0.874% | 0.871% | 0.882% |
| 8A ^a | Terminal Body Wt (g) | 325.1 ± 19.36 | 319.1 ± 16.43 | 317.6 ± 7.60 | 314.8 ± 17.74 | 312.6 ± 15.87** |
| | Liver (g) | 13.9 ± 1.28 | 13.6 ± 1.21 | 13.3 ± 0.84 | 13.3 ± 0.55 | 14.5 ± 1.19 ** |
| | (relative to bw) | 4.28% | 4.26% | 4.19% | 4.22% | 4.64% |
| | Adrenals (mg) | 51.2 ± 6.41 | 48.5 ± 6.28 | 58.6 ± 7.38 | 60.2 ± 5.85 | 62.3 ± 6.01 |
| | (relative to bw) | 0.0157% | 0.0152% | 0.0185% | 0.0191% | 0.0199% |
| | Kidneys (mg) | 2198.4 ± 186.19 | 2179.1 ± 197.50 | 2072.8 ± 129.05 | 2134.1 ± 193.25 | 2003.3 ± 194.90 |
| | (relative to bw) | 0.676% | 0.683% | 0.653% | 0.678% | 0.641% |
| 8B ^a | Terminal Body Wt (g) | 333.2 ± 17.58 | 330.6 ± 17.91 | 329.1 ± 13.81 | 319.7 ± 11.30 | 310.9 ± 13.99** |
| | Liver (g) | 13.1 ± 1.1 | 13.5 ± 1.0 | 13.2 ± 0.5 | 13.3 ± 0.7 | 13.7 ± 1.3 * |
| | (relative to bw) | 3.94% | 4.07% | 4.00% | 4.16% | 4.40% |
| | Adrenals (mg) | 57.1 ± 5.6 | 50.6 ± 5.4 | 54.4 ± 7.2 | 57.5 ± 8.2 | 69.7 ± 9.6 ** |
| | (relative to bw) | 0.0171% | 0.0153% | 0.0165% | 0.0180% | 0.0224% |
| | Kidneys (mg) | 2270.8 ± 168.9 | 2334.1 ± 169.1 | 2121.8 ± 106.0 | 2145.6 ± 183.3 | 2036.5 ± 60.8 |
| | (relative to bw) | 0.681% | 0.706% | 0.645% | 0.671% | 0.655% |
| 9 | Terminal Body Wt (g) | 338.0 ± 19.10 | 336.2 ± 14.77 | 335.3 ± 15.56 | 329.7 ± 8.80 | 331.5 ± 16.39 |
| | Liver (g) | 17.2 ± 1.33 | 16.3 ± 0.91 | 16.8 ± 0.84 | 18.0 ± 1.07 ** | 18.4 ± 1.73 ** |
| | (relative to bw) | 5.09% | 4.85% | 5.01% | 5.46% | 5.55% |
| | Adrenals (mg) | 56.6 ± 4.70 | 56.7 ± 5.20 | 53.5 ± 10.49 | 61.3 ± 14.05 | 67.2 ± 11.72 |
| | (relative to bw) | 0.0167% | 0.0169% | 0.0160% | 0.0186% | 0.0203% |
| | Kidneys (mg) | 2398.6 ± 169.06 | 2525.8 ± 138.74 | 2394.0 ± 111.39 | 2529.0 ± 98.65 | 2483.6 ± 166.40 |
| | (relative to bw) | 0.710% | 0.751% | 0.714% | 0.767% | 0.749% |

*, ** Significantly different from control at P<0.05 and P<0.01, respectively, using T-test pairwise comparisons.

^a Laboratory 8 performed two studies as several mortalities occurred reducing group size in the first study due to gavage errors.

Suppl. Material Table 13. Optional organ weights linuron (LIN) studies (mean ± SD).

| Lab | Testosterone Prop. (mg/kg-bw/d) | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 |
|-----|---------------------------------|-----------------|-----------------|-----------------|----------------|-----------------|
| | Linuron (mg/kg-bw/d) | 0 | 3 | 10 | 30 | 100 |
| 1 | Terminal Body Wt (g) | 219.9 ± 11.37 | 221.7 ± 17.58 | 218.9 ± 16.63 | 218.2 ± 11.13 | 203.1 ± 11.04 |
| | Liver (g) | 6.6 ± 0.29 | 6.4 ± 0.44 | 6.7 ± 0.78 | 6.5 ± 0.48 | 6.3 ± 0.67 |
| | (relative to bw) | 3.00% | 2.89% | 3.06% | 2.98% | 3.10% |
| | Adrenals (mg) | 69.3 ± 12.79 | 60.3 ± 7.17 | 67.0 ± 16.96 | 68.5 ± 7.31 | 63.7 ± 15.07 |
| | (relative to bw) | 0.0315% | 0.0272% | 0.0306% | 0.0314% | 0.0314% |
| | Kidneys (mg) | 1681.7 ± 75.74 | 1761.7 ± 132.73 | 1665.0 ± 115.89 | 1633.3 ± 77.11 | 1626.7 ± 139.67 |
| | (relative to bw) | 0.7648% | 0.7946% | 0.7606% | 0.7485% | 0.8009% |
| 4 | Terminal Body Wt (g) | 372.3 ± 14.74 | 364.7 ± 15.59 | 355.7 ± 17.42 | 351.8 ± 14.84 | 330.9 ± 12.86 |
| | Liver (g) | 15.7 ± 1.34 | 15.6 ± 1.54 | 14.7 ± 1.30 | 13.9 ± 1.27 | 15.7 ± 1.34 |
| | (relative to bw) | 4.22% | 4.28% | 4.13% | 3.95% | 4.74% |
| | Adrenals (mg) | 64.6 ± 11.20 | 58.3 ± 7.30 | 57.3 ± 4.89 | 64.1 ± 4.68 | 64.6 ± 11.20 |
| | (relative to bw) | 0.0174% | 0.0160% | 0.0161% | 0.0182% | 0.0195% |
| | Kidneys (mg) | 2573.5 ± 145.73 | 2522.5 ± 125.99 | 2345.0 ± 183.04 | 2404.1 ± 77.97 | 2573.5 ± 145.73 |
| | (relative to bw) | 0.6912% | 0.6917% | 0.6593% | 0.6834% | 0.7777% |
| 5 | Terminal Body Wt (g) | 281.2 ± 18.73 | 284.0 ± 22.71 | 280.0 ± 21.48 | 277.2 ± 18.17 | 264.2 ± 10.85 |
| | Liver (g) | 9.9 ± 1.49 | 11.0 ± 1.32 | 10.3 ± 1.21 | 9.6 ± 1.06 | 9.0 ± 0.92 |
| | (relative to bw) | 3.52% | 3.87% | 3.68% | 3.46% | 3.41% |
| | Adrenals (mg) | 57.2 ± 11.04 | 63.5 ± 9.80 | 47.5 ± 8.66 | 60.4 ± 14.94 | 66.1 ± 10.22 |
| | (relative to bw) | 0.0203% | 0.0224% | 0.0170% | 0.0218% | 0.0250% |
| | Kidneys (mg) | 1607.0 ± 199.61 | 1615.3 ± 171.69 | 1558.4 ± 131.98 | 1563.7 ± 95.03 | 1539.7 ± 96.96 |
| | (relative to bw) | 0.5715% | 0.5688% | 0.5566% | 0.5641% | 0.5828% |
| 6 | Terminal Body Wt (g) | 306.5 ± 9.96 | 310.5 ± 12.69 | 305.5 ± 8.63 | 302.3 ± 13.13 | 291.8 ± 17.62 |
| | Liver (g) | 15.1 ± 2.021 | 17.3 ± 2.42 | 16.9 ± 1.33 | 14.9 ± 1.89 | 15.8 ± 2.34 |
| | (relative to bw) | 4.93% | 5.57% | 5.53% | 4.93% | 5.41% |
| | Adrenals (mg) | 57.9 ± 6.5 | 64.9 ± 8.82 | 62.7 ± 18.42 | 59.1 ± 8.30 | 63.9 ± 7.82 |
| | (relative to bw) | 0.0189% | 0.0209% | 0.0205% | 0.0196% | 0.0219% |
| | Kidneys (mg) | 2622.7 ± 288.08 | 2768.1 ± 87.85 | 2674.7 ± 197.14 | 2639.9 ± 73.07 | 2699.5 ± 309.99 |
| | (relative to bw) | 0.8557% | 0.8915% | 0.8755% | 0.8733% | 0.9251% |

*,** Significantly different from control at P<0.05 and P<0.01, respectively, using T-test pairwise comparisons.

Suppl. Material Table 14. Optional organ weights finasteride (FIN) studies (mean ± SD).

| Lab | Testoster. Prop. (mg/kg-bw/d) | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 |
|-----|-------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| | Finasteride (mg/kg-bw/d) | 0 | 0.2 | 1 | 5 | 25 |
| 2 | Terminal Body Wt (g) | 301.2 ± 20.90 | 287.9 ± 18.69 | 288.5 ± 12.64 | 283.9 ± 21.19 | 293.2 ± 6.79 |
| | Liver (g) | 12.2 ± 1.03 | 11.5 ± 1.59 | 11.6 ± 1.52 | 11.3 ± 1.01 | 12.5 ± 0.70 |
| | (relative to bw) | 4.05% | 3.99% | 4.02% | 3.98% | 4.26% |
| | Adrenals (mg) | 55.3 ± 7.75 | 54.8 ± 9.64 | 45.7 ± 12.18 | 55.8 ± 4.38 | 52.3 ± 11.30 |
| | (relative to bw) | 0.0184% | 0.0190% | 0.0158% | 0.0197% | 0.0178% |
| | Kidneys (mg) | 2194.7 ± 149.79 | 1947.8 ± 185.24 | 1988.0 ± 138.86 | 1961.7 ± 211.31 | 2013.3 ± 109.20 |
| | (relative to bw) | 0.7287% | 0.6766% | 0.6891% | 0.6910% | 0.6867% |
| 5 | Terminal Body Wt (g) | 272.8 ± 21.48 | 273.5 ± 17.24 | 278.0 ± 22.53 | 276.0 ± 22.92 | 275.0 ± 15.10 |
| | Liver (g) | 10.8 ± 1.85 | 10.6 ± 1.41 | 10.7 ± 1.86 | 10.5 ± 1.13 | 10.8 ± 1.23 |
| | (relative to bw) | 3.96% | 3.88% | 3.85% | 3.80% | 3.93% |
| | Adrenals (mg) | 57.6 ± 10.52 | 58.5 ± 7.09 | 52.8 ± 5.85 | 52.5 ± 4.64 | 52.7 ± 11.18 |
| | (relative to bw) | 0.0211% | 0.0214% | 0.0190% | 0.0190% | 0.0192% |
| | Kidneys (mg) | 1724.7 ± 120.74 | 1718.0 ± 115.96 | 1680.7 ± 185.77 | 1750.9 ± 126.18 | 1669.3 ± 182.22 |
| | (relative to bw) | 0.6322% | 0.6282% | 0.6046% | 0.6344% | 0.6070% |
| 6 | Terminal Body Wt (g) | 311.9 ± 18.24 | 316.7 ± 12.13 | 317.3 ± 14.90 | 313.9 ± 10.83 | 314.3 ± 13.60 |
| | Liver (g) | 15.8 ± 1.65 | 16.5 ± 1.98 | 16.6 ± 1.66 | 16.7 ± 1.98 | 16.7 ± 1.96 |
| | (relative to bw) | 5.07% | 5.21% | 5.23% | 5.32% | 5.31% |
| | Adrenals (mg) | 59.3 ± 9.62 | 57.4 ± 6.53 | 53.6 ± 13.68 | 53.7 ± 7.92 | 51.7 ± 6.13 |
| | (relative to bw) | 0.0190% | 0.0181% | 0.0169% | 0.0171% | 0.0164% |
| | Kidneys (mg) | 2688.9 ± 246.29 | 2666.2 ± 236.50 | 2751.9 ± 155.57 | 2643.7 ± 178.06 | 2716.7 ± 272.94 |
| | (relative to bw) | 0.8621% | 0.8419% | 0.8673% | 0.8422% | 0.8644% |
| 9 | Terminal Body Wt (g) | 322.3 ± 13.08 | 333.5 ± 14.10 | 330.3 ± 11.38 | 338.2 ± 14.47 | 334.3 ± 13.44 |
| | Liver (g) | 15.7 ± 1.06 | 16.9 ± 1.11 | 16.7 ± 1.21 | 17.4 ± 1.23 | 17.4 ± 0.73 |
| | (relative to bw) | 4.87% | 5.07% | 5.06% | 5.14% | 5.20% |
| | Adrenals (mg) | 57.1 ± 6.19 | 54.7 ± 5.63 | 50.2 ± 3.16 | 50.5 ± 3.54 | 53.6 ± 2.83 |
| | (relative to bw) | 0.0177% | 0.0164% | 0.0152% | 0.0149% | 0.0160% |
| | Kidneys (mg) | 2423.1 ± 188.53 | 2488.1 ± 195.63 | 2423.4 ± 179.53 | 2496.5 ± 161.99 | 2494.0 ± 190.43 |
| | (relative to bw) | 0.7518% | 0.7461% | 0.7337% | 0.7382% | 0.7460% |

*, ** Significantly different from control at P<0.05 and P<0.01, respectively, using T-test pairwise comparisons.

Section III. EHP 9666: OECD Validation of Rat Hershberger Assay: Phase-2 Dose Response Studies
Comparison of the tissue LOELs for each test substance in Phase-2.

This section contains the following tables of detailed data for Phase-2 of the OECD Hershberger Validation Program.

Suppl. Material Table 15. LOELs for each mandatory tissue at given agonist doses in Phase-2.

Suppl. Material Table 16. LOELs for each mandatory tissue for vinclozolin antiandrogen doses in Phase-2.

Suppl. Material Table 17. LOELs for each mandatory tissue for *p,p'*-DDE antiandrogen doses in Phase-2.

Suppl. Material Table 18. LOELs for each mandatory tissue at antiandrogen doses for procymidone, linuron, and finasteride in Phase-2.

Suppl. Material Table 15. LOELs for each mandatory tissue at given agonist doses in Phase-2.^a

| | Methyl Testosterone (mg/kg-bw/d) | | | | No LOEL observed |
|------------------|----------------------------------|-----|---|----|------------------|
| | 0.05 | 0.5 | 5 | 50 | |
| Ventral prostate | 0 | 0 | 3 | 1 | 0 |
| SVCG | 0 | 0 | 1 | 3 | 0 |
| LABC | 0 | 0 | 4 | 0 | 0 |
| Glans penis | 0 | 0 | 4 | 0 | 0 |
| Cowper's Glands | 0 | 0 | 2 | 2 | 0 |

| | Methyl Testosterone (mg/kg-bw/d) | | | | No LOEL observed |
|------------------|----------------------------------|---|----|----|------------------|
| | 0.5 | 2 | 10 | 40 | |
| Ventral prostate | 0 | 1 | 3 | 0 | 0 |
| SVCG | 0 | 1 | 2 | 1 | 0 |
| LABC | 0 | 3 | 1 | 0 | 0 |
| Glans penis | 0 | 1 | 2 | 1 | 0 |
| Cowper's Glands | 0 | 3 | 0 | 1 | 0 |

| | Trenbolone (mg/kg-bw/d) | | | | No LOEL observed |
|------------------|-------------------------|-----|---|----|------------------|
| | 0.3 | 1.5 | 8 | 40 | |
| Ventral prostate | 0 | 0 | 1 | 2 | 0 |
| SVCG | 0 | 0 | 0 | 3 | 0 |
| LABC | 0 | 0 | 1 | 2 | 0 |
| Glans penis | 0 | 0 | 1 | 2 | 0 |
| Cowper's Glands | 0 | 0 | 0 | 3 | 0 |

^a Using the t-test statistical approach.

Suppl. Material Table 16. LOELs for each mandatory tissue for vinclozolin doses in Phase-2.^a

| | Vinclozolin (mg/kg-bw/d) | | | | No LOEL observed |
|-------------------|--------------------------|----|----|-----|------------------|
| | 3 | 10 | 30 | 100 | |
| 0.2 mg/kg-bw/d TP | | | | | |
| Ventral prostate | 1 | 2 | 0 | 1 | 0 |
| SVCG | 0 | 1 | 3 | 0 | 0 |
| LABC | 0 | 1 | 3 | 0 | 0 |
| Glans penis | 0 | 1 | 3 | 0 | 0 |
| Cowper's Glands | 0 | 2 | 2 | 0 | 0 |
| 0.4 mg/kg-bw/d TP | | | | | |
| Ventral prostate | 0 | 0 | 3 | 1 | 0 |
| SVCG | 0 | 0 | 4 | 0 | 0 |
| LABC | 0 | 0 | 4 | 0 | 0 |
| Glans penis | 0 | 0 | 1 | 2 | 0 |
| Cowper's Glands | 0 | 0 | 1 | 3 | 0 |

^a Using the t-test statistical approach.

Suppl. Material Table 17. LOELs for each mandatory tissue for *p,p'*-DDE antiandrogen doses in Phase-2.^a

| | <i>p,p'</i> -DDE (mg/kg-bw/d) | | | | No LOEL observed |
|-------------------|-------------------------------|----|----|-----|------------------|
| | 3 | 10 | 30 | 100 | |
| 0.2 mg/kg-bw/d TP | | | | | |
| Ventral prostate | 0 | 0 | 3 | 1 | 0 |
| SVCG | 0 | 0 | 2 | 2 | 0 |
| LABC | 0 | 0 | 4 | 0 | 0 |
| Glans penis | 0 | 0 | 0 | 4 | 0 |
| Cowper's Glands | 0 | 0 | 4 | 0 | 0 |
| | <i>p,p'</i> -DDE (mg/kg-bw/d) | | | | |
| | 5 | 16 | 50 | 160 | |
| 0.4 mg/kg-bw/d TP | | | | | |
| Ventral prostate | 0 | 0 | 3 | 1 | 0 |
| SVCG | 0 | 0 | 2 | 2 | 0 |
| LABC | 0 | 0 | 3 | 0 | 0 |
| Glans penis | 0 | 0 | 0 | 3 | 0 |
| Cowper's Glands | 0 | 0 | 4 | 0 | 0 |

^a Using the t-test statistical approach.

Suppl. Material Table 18. LOELs for each mandatory tissue at antiandrogen doses for procymidone, linuron, and finasteride in Phase-2.^a

| | Procymidone (mg/kg-bw/d) | | | | No LOEL observed |
|------------------|--------------------------|----|----|-----|------------------|
| | 3 | 10 | 30 | 100 | |
| Ventral prostate | 0 | 4 | 1 | 0 | 0 |
| SVCG | 0 | 2 | 3 | 0 | 0 |
| LABC | 1 | 2 | 2 | 0 | 0 |
| Glans penis | 0 | 1 | 2 | 0 | 2 |
| Cowper's Glands | 1 | 2 | 1 | 0 | 0 |
| | Linuron (mg/kg-bw/d) | | | | |
| | 3 | 10 | 30 | 100 | No LOEL observed |
| Ventral prostate | 0 | 0 | 1 | 2 | 1 |
| SVCG | 0 | 0 | 2 | 2 | 0 |
| LABC | 0 | 0 | 1 | 2 | 1 |
| Glans penis | 0 | 0 | 0 | 1 | 3 |
| Cowper's Glands | 0 | 0 | 0 | 3 | 1 |
| | Finasteride (mg/kg-bw/d) | | | | |
| | 0.2 | 1 | 5 | 25 | No LOEL observed |
| Ventral prostate | 0 | 3 | 0 | 0 | 0 |
| SVCG | 1 | 2 | 0 | 0 | 0 |
| LABC | 3 | 2 | 0 | 0 | 0 |
| Glans penis | 0 | 3 | 2 | 0 | 0 |
| Cowper's Glands | 2 | 3 | 0 | 0 | 0 |

^a Using the t-test statistical approach.

Section IV. EHP 9666: OECD Validation of Rat Hershberger Assay: Phase-2 Dose Response Studies
Benchmark dose calculations for the five mandatory sex accessory target tissues for each laboratory.

This section contains the following tables of detailed data for Phase-2 of the OECD Hershberger Validation Program.

Suppl. Material Table 19. Benchmark doses (BMDs) for 17 α -methyltestosterone: Mandatory tissue by individual laboratory and combined.

Suppl. Material Table 20. Benchmark doses (BMDs) for trenbolone: Mandatory tissue by individual laboratory and combined.

Suppl. Material Table 21. Benchmark doses (BMDs) for vinclozolin: Mandatory tissue by individual laboratory and combined.

Suppl. Material Table 22. Benchmark doses (BMDs) for *p,p'*-DDE: Mandatory tissue by individual laboratory and combined.

Suppl. Material Table 23. Benchmark doses (BMDs) for procymidone: Mandatory tissue by individual laboratory and combined.

Suppl. Material Table 24. Benchmark doses (BMDs) for linuron: Mandatory tissue by individual laboratory and combined.

Suppl. Material Table 25. Benchmark doses (BMDs) for finasteride: Mandatory tissue by individual laboratory and combined.

Suppl. Material Table 19: Benchmark doses (BMDs) for 17 α -methyltestosterone:
Mandatory tissue by individual laboratory and combined.

| Lab | BMD (BMDL*) mg/kg-bw/day | | | | | |
|---------|--------------------------|-------------|-------------|-------------|-------------|-------------|
| | VP | SVCG | LABC | GP | COWS | |
| Stage-1 | 11 | 0.45 (0.11) | 3.3 (1.2) | 1.1 (0.36) | 1.3 (0.27) | 2.0 (0.38) |
| | 13 | 0.96 (0.40) | 2.8 (1.0) | 0.79 (0.25) | 0.24 (0.12) | 0.90 (0.28) |
| | 15 | 0.75 (0.22) | 1.3 (0.22) | 1.5 (0.40) | 0.47 (0.22) | 0.47 (0.12) |
| | 16 | 3.1 (1.2) | 4.4 (2.3) | 1.4 (0.57) | 1.6 (0.57) | 4.6 (1.9) |
| | Combined | 0.51 (0.37) | 0.94 (0.66) | 0.95 (0.67) | 0.91 (2.9) | 0.53 (0.39) |
| Stage-2 | 2 | 2.1 (0.34) | 4.9 (0.78) | 2.4 (0.98) | 1.2 (0.55) | 2.5 (0.64) |
| | 4 | 1.3 (0.24) | 2.9 (0.78) | 0.53 (0.19) | 1.0 (0.49) | 0.63 (0.16) |
| | 6 | 4.6 (1.2) | 3.6 (0.98) | 1.6 (0.35) | 2.5 (0.82) | 2.2 (0.29) |
| | 8 | 1.7 (0.65) | 4.5 (1.5) | 0.38 (0.11) | 2.5 (0.40) | 0.30 (NA**) |
| | Combined | 3.0 (1.3) | 4.8 (2.6) | 2.0 (0.69) | 1.8 (0.89) | 1.7 (0.65) |

*BMDL = 95% Lower Confidence Limit on the BMD

**NA = Lower bound computation did not converge

Suppl. Material Table 20: Benchmark doses (BMDs) for trenbolone:
Mandatory tissue by individual laboratory and combined.

| Lab | BMD (BMDL*) mg/kg-bw/day | | | | |
|----------|--------------------------|------------|------------|------------|-------------|
| | VP | SVCG | LABC | GP | COWS |
| 1 | 8.7 (2.2) | 9.2 (1.3) | 4.7 (1.3) | 30.0 (2.0) | 13.4 (2.9) |
| 3 | 33.2 (2.5) | 14.3 (2.5) | 5.9 (1.8) | 8.4 (1.4) | 26.9 (18.0) |
| 7 | 1.4 (0.37) | 10.0 (1.8) | 1.5 (0.26) | 1.5 (0.48) | 10.6 (1.7) |
| Combined | 8.8 (2.2) | 13.8 (4.1) | 5.1 (1.5) | 7.7 (3.2) | 15.9 (5.3) |

*BMDL = 95% Lower Confidence Limit on the BMD

Suppl. Material Table 21: Benchmark doses (BMDs) for vinclozolin: Mandatory tissue by individual laboratory and combined.

| Lab | BMD (BMDL*) mg/kg-bw/day | | | | | |
|---------|--------------------------|-------------|-------------|-------------|-------------|-------------|
| | VP | SVCG | LABC | GP | COWS | |
| Stage-1 | 10 | 1.8 (0.44) | 1.4 (0.37) | 1.8 (0.40) | 10.5 (2.9) | 6.0 (1.7) |
| | 11 | 13.8 (4.4) | 2.7 (0.74) | 4.4 (0.76) | 1.5 (0.78) | 1.7 (0.59) |
| | 13 | 0.60 (0.34) | 0.23 (0.15) | 0.70 (NA**) | 0.72 (0.25) | 1.2 (0.50) |
| | 14 | 0.17 (0.12) | 2.8 (0.76) | 2.3 (0.65) | 14.9 (5.4) | 2.0 (0.56) |
| | Combined | 2.3 (1.2) | 2.7 (1.2) | 4.6 (1.9) | 7.6 (2.7) | 3.6 (1.8) |
| Stage-2 | 1 | 6.7 (1.7) | 6.7 (1.8) | 4.5 (1.4) | 2.6 (0.61) | 3.9 (1.2) |
| | 3 | 7.0 (1.4) | 6.0 (1.7) | 5.1 (1.1) | 76.4 (21.2) | 15.7 (5.0) |
| | 5 | 22.6 (4.0) | 3.6 (0.60) | 2.3 (0.66) | 42.0 (4.5) | 15.7 (1.8) |
| | 7 | 0.86 (0.47) | 5.5 (1.4) | 2.3 (0.56) | 24.4 (4.6) | 81.7 (20.1) |
| | Combined | 9.2 (3.1) | 12.2 (5.1) | 8.7 (4.0) | 36.0 (9.8) | 35.1 (11.5) |

*BMDL = 95% Lower Confidence Limit on the BMD

**NA = Lower bound computation did not converge

Suppl. Material Table 22: Benchmark doses (BMDs) for *p,p'*-DDE: Mandatory tissue by individual laboratory and combined.

| Lab | BMD (BMDL*) mg/kg-bw/day | | | | | | |
|---------|--------------------------|-------------|-------------|-------------|-------------|-------------|------------|
| | VP | SVCG | LABC | GP | COWS | LIVER | |
| Stage-1 | 10 | 2.2 (0.62) | 5.1 (1.4) | 70.0 (23.4) | 57.0 (10.3) | 3.7 (0.97) | - |
| | 11 | 6.4 (1.0) | 14.2 (4.1) | 8.5 (2.3) | 32.1 (12.2) | 36.7 (5.8) | - |
| | 12 | 71.0 (24.3) | 2.9 (0.90) | 25.7 (2.5) | 75.7 (50.4) | 45.9 (13.8) | - |
| | 14 | 24.6 (8.5) | 13.7 (6.1) | 14.1 (7.5) | 22.8 (8.8) | 40.2 (9.1) | - |
| | 16 | 2.7 (0.78) | 8.7 (2.5) | 3.1 (0.70) | 11.1 (1.6) | 8.0 (1.0) | 2.2 (0.71) |
| | Combined | 16.1 (6.2) | 12.5 (5.4) | 13.0 (5.1) | 95.6 (71.5) | 26.5 (11.3) | 2.2 (0.71) |
| Stage-2 | 3 | 7.4 (2.4) | 12.8 (4.9) | 3.5 (0.95) | 22.8 (4.7) | 1.4 (0.47) | 3.6 (1.7) |
| | 4 | 45.7 (11.2) | 35.5 (6.7) | 14.6 (5.0) | 64.1 (16.4) | 6.4 (1.8) | 3.4 (0.93) |
| | 8 | 12.7 (4.2) | 14.2 (3.9) | 9.4 (1.2) | 39.2 (3.7) | 10.7 (2.0) | 1.5 (0.79) |
| | 9 | 2.6 (1.3) | 5.2 (0.97) | 7.3 (1.8) | 33.5 (11.4) | 5.8 (1.2) | 1.4 (0.55) |
| | Combined | 23.6 (10.1) | 22.1 (10.8) | 17.9 (5.7) | 54.2 (21.7) | 11.8 (5.8) | 3.9 (2.7) |

*BMDL = 95% Lower Confidence Limit on the BMD

Suppl. Material Table 23: Benchmark doses (BMDs) for procymidone: Mandatory tissue by individual laboratory and combined.

| Lab | BMD (BMDL*) mg/kg-bw/day | | | | |
|----------|--------------------------|-------------|-------------|-------------|-------------|
| | VP | SVCG | LABC | GP | COWS |
| 2 | 3.5 (0.84) | 10.0 (2.1) | 18.2 (5.4) | 44.0 (8.2) | 33.6 (4.4) |
| 7 | 1.6 (0.83) | 1.1 (0.57) | 3.0 (1.4) | 10.6 (3.8) | 4.4 (1.9) |
| 8-A | 0.48 (0.28) | 3.4 (0.90) | 1.6 (0.50) | 2.6 (0.78) | 0.46 (0.27) |
| 8-B | 0.56 (NA**) | 0.30 (NA) | 0.31 (NA) | 1.6 (0.81) | 6.3 (1.2) |
| 9 | 1.4 (0.47) | 0.47 (0.27) | 0.62 (0.35) | 6.8 (2.6) | 0.25 (0.17) |
| Combined | 1.5 (1.1) | 2.2 (1.4) | 5.9 (3.8) | 17.8 (10.0) | 3.7 (2.5) |

*BMDL = 95% Lower Confidence Limit on the BMD

**NA = Lower bound computation did not converge

Suppl. Material Table 24: Benchmark doses (BMDs) for linuron: Mandatory tissue by individual laboratory and combined.

| Lab | BMD (BMDL*) mg/kg-bw/day | | | | |
|----------|--------------------------|-------------|-------------|-------------|-------------|
| | VP | SVCG | LABC | GP | COWS |
| 1 | 14.9 (5.0) | 13.2 (5.3) | 12.9 (5.0) | 12.6 (2.6) | 25.5 (6.6) |
| 4 | 44.1 (17.5) | 72.1 (19.4) | 9.5 (2.1) | 91.4 (28.3) | 44.2 (8.0) |
| 5 | 7.7 (2.0) | 0.85 (0.40) | 7.1 (2.1) | 78.4 (30.2) | 13.1 (2.1) |
| 6 | 84.2 (20.9) | 16.5 (3.6) | 80.6 (53.8) | No D-R** | No D-R |
| Combined | 38.3 (19.1) | 22.0 (8.2) | 31.3 (10.6) | 100 (48.1) | 44.8 (15.6) |

*BMDL = 95% Lower Confidence Limit on the BMD

** No D-R = No Dose-Response relationship

Suppl. Material Table 25: Benchmark doses (BMDs) for finasteride: Mandatory tissue by individual laboratory and combined.

| Lab | BMD (BMDL*) mg/kg-bw/day | | | | |
|----------|--------------------------|-------------|-------------|-------------|-------------|
| | VP | SVCG | LABC | GP | COWS |
| 2 | 0.55 (0.27) | 1.1 (0.48) | 2.7 (0.94) | 12.9 (2.7) | 0.96 (0.43) |
| 5 | 1.5 (0.58) | 1.7 (0.63) | 0.83 (0.37) | 0.79 (0.31) | 0.29 (0.15) |
| 6 | 0.66 (0.31) | 1.2 (0.51) | 15.2 (2.7) | No D-R** | 1.3 (0.57) |
| 9 | 0.50 (0.24) | 0.40 (0.20) | 1.2 (0.52) | 1.4 (0.59) | 0.26 (0.14) |
| Combined | 0.87 (0.57) | 1.4 (0.85) | 8.8 (4.0) | 20.6 (6.8) | 0.77 (0.51) |

*BMDL = 95% Lower Confidence Limit on the BMD

** No D-R = No Dose-Response relationship