**Table S1.** The mean and standard deviation for each endpoint measured during medaka multi-generational test conducted at MED at all measured concentrations levels of 4tOP. “X” = no fish available; “-“ = measurement not in specific test design.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **4tOP MED** | | | | | | | | | | | | | |
|  | **control** | | **6 μg/L** | | **13 μg/L** | | **25 μg/L** | | **51 μg/L** | | **102 μg/L** | | |
| **FECUNDITY (eggs per pair-day)** | | | | | | | | | | | | | |
| F0 | 23.9 ± 2.9 | | 22.7 ± 6.2 | | 18.8 ± 10.0 | | 14.8 ± 2.6 | | 17.9 ± 6.0 | | 18.1 ± 9.6 | | |
| F1 | 17.4 ± 4.1 | | 23.6 ± 9.1 | | 22.6 ± 4.8 | | 22.3 ± 3.2 | | 14.4 ± 8.5 | | 1.1 ± 1.0 | | |
| F2 | 19.5 ± 12.1 | | 22.8 ± 9.2 | | 14.0 ± 10.8 | | 23.6 ± 4.2 | | 8.6 ± 8.2 | | X | | |
| **FERTILITY** | | | | | | | | | | | | | |
| F0 | 96% | | 94% | | 94% | | 93% | | 97% | | 91% | | |
| F1 | 89 ± 7% | | 83 ± 3% | | 94 ± 3% | | 93 ± 4% | | 71 ± 4% | | 16 ± 12% | | |
| F2 | 78 ± 4% | | 80 ± 4% | | 43 ± 4% | | 95 ± 6% | | 27 ± 38% | | X | | |
| **HATCH** | | | | | | | | | | | | | |
| F1 | 85 ± 9% | | 76 ± 26% | | 88 ± 7% | | 88 ± 13% | | 78 ± 13% | | 41 ± 38% | | |
| F2 | 87 ± 10% | | 87 ± 21% | | 82 ± 8% | | 88 ± 5% | | 93 ± 9% | | X | | |
| **LARVAL SURVIVAL** | | | | | | | | | | | | | |
| F1 | - | | - | | - | | - | | - | | - | | |
| F2 | - | | - | | - | | - | | - | | - | | |
| **SUBADULT SURVIVAL** | | | | | | | | | | | | | |
| F1 | 97 ± 5% | | 97 ± 5% | | 98 ± 4% | | 98 ± 4% | | 100% | | 90 ± 4% | | |
| F2 | 98 ± 5% | | 100% | | 98 ± 4% | | 100% | | 98 ± 4% | | X | | |
|  | | | | | | | | | | | | | |
|  | **control** | | **6 μg/L** | | **13 μg/L** | | **25 μg/L** | | **51 μg/L** | | **102 μg/L** | | |
|  | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | |
| **ADULT SURVIVAL** | | | | | | | | | | | | | |
| F0 | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | | 100% |
| F1 | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 83% | 83% | 83% | 83% | | 100% |
| F2 | 83% | 100% | 83% | 100% | 67% | 100% | 100% | 100% | 100% | 50% | X | | X |
| **ADULT WEIGHT (mg)** | | | | | | | | | | | | | |
| F0 | 480±50 | 374±39 | 455±50 | 410±77 | 548±81 | 451±62 | 568±94 | 416±75 | 528±80 | 374±71 | 585±90 | 439±85 | |
| F1 | 442±82 | 358±193 | 393±72 | 297±62 | 426±61 | 404±26 | 417±81 | 346±60 | 405±101 | 429±149 | 530±72 | 413±147 | |
| F2 | 525±179 | 378±85 | 376±27 | 363±49 | 463±129 | 463±124 | 445±62 | 399±33 | 580±106 | 456 ± 55 | X | X | |
| **SUBADULT WEIGHT (mg)** | | | | | | | | | | | | | |
| F1 | 94 ± 35 | 74 ± 17 | 99 ± 27 | 103±24 | 115±27 | 123±13 | 105±34 | 88 ± 19 | 98 ± 34 | 102±29 | 122±48 | 65 ± 35 | |
| F2 | 109±22 | 99 ± 29 | 109±27 | 97 ± 22 | 107±24 | 106±16 | 118±39 | 97 ± 30 | 107±25 | 109±24 | X | X | |
| **ADULT LENGTH (mm)** | | | | | | | | | | | | | |
| F0 | 35 ± 1 | 34 ± 1 | 35 ± 1 | 36 ± 2 | 37 ± 1 | 36 ± 1 | 37 ± 2 | 35 ± 2 | 35 ± 2 | 35 ± 2 | 37 ± 2 | 35 ± 2 | |
| F1 | 34 ± 1 | 32 ± 1 | 34 ± 2 | 33 ± 2 | 34 ± 1 | 35 ± 1 | 34 ± 1 | 34 ± 1 | 33 ± 2 | 36 ± 2 | 34 ± 1 | 33 ± 5 | |
| F2 | 36 ± 4 | 35 ± 2 | 32 ± 1 | 34 ± 1 | 34 ± 2 | 35 ± 2 | 34 ± 1 | 35 ± 1 | 35 ± 2 | 36 ± 2 | X | X | |
| **SUBADULT LENGTH (mm)** | | | | | | | | | | | | | |
| F1 | 20 ± 2 | 20 ± 1 | 21 ± 2 | 21 ± 2 | 21 ± 2 | 22 ± 0 | 21 ± 3 | 20 ± 2 | 20 ± 3 | 21 ± 2 | 22 ± 2 | 18 ± 3 | |
| F2 | 21 ± 2 | 20 ± 2 | 21 ± 2 | 20 ± 2 | 21 ± 2 | 21 ± 1 | 21 ± 2 | 20 ± 3 | 21 ± 2 | 21 ± 1 | X | X | |
| **ADULT VITELLOGENIN (copies per ng total RNA)** | | | | | | | | | | | | | |
| F0 | 7.8x105 ± 7.4x105 | 9.3x103 ± 1.2x104 | 9.4x105± 6.5x105 | 1.1x104± 1.6x104 | 1.0x106± 9.1x105 | 4.6x104± 9.0x104 | 9.6x105± 4.1x105 | 5.1x104± 7.9x104 | 1.1x106± 4.3x105 | 3.6x105± 2.1x105 | 9.1x105± 7.1x105 | 5.4x105± 5.5x105 | |
| F1 | 2.0x106± 1.3x106 | 5.8x104± 1.1x105 | 1.6x106± 8.3x105 | 7.4x103± 3.9x103 | 1.9x106± 1.6x106 | 1.5x104± 3.0x104 | 1.5x106± 4.3x105 | 4.2x104± 3.7x104 | 1.4x106± 8.0x105 | 5.0x105± 3.1x105 | 1.5x106± 6.6x105 | 1.4x106± 6.9x105 | |
| F2 | 1.7x106 ± 1.6x106 | 6.7x103 ± 1.0x104 | 4.6x106± 6.3x106 | 5.1x103± 6.1x103 | 4.9x106 ± 7.7x106 | 1.3x104 ± 1.9x104 | 3.0x106± 1.6x106 | 2.3x104± 3.8x104 | 2.4x106 ± 1.6x106 | 6.5x105 ± 1.0x106 | X | X | |
|  | **SUBADULT VITELLOGENIN (copies per ng total RNA)** | | | | | | | | | | | | |
| F1 | 2.0x105 ± 1.8x105 | 1.0x103 ± 1.9x103 | 1.9x105± 1.9x105 | 1.0x103± 2.1x103 | 2.7x105 ± 4.0x105 | 1.7x103 ± 2.8x103 | 3.9x105± 3.8x105 | 7.0x103± 2.2x104 | 4.4x105 ± 4.3x105 | 1.0x105 ± 2.8x105 | 7.8x105± 5.2x105 | 1.7x105 ± 8.1x104 | |
| F2 | 2.3x105 ± 2.4x105 | 3.8x103 ± 1.7x104 | 2.7x105± 3.0x105 | 5.2x102± 4.7x102 | 2.0x105 ± 3.4x105 | 3.4x102 ± 1.4x102 | 4.9x105± 5.5x105 | 1.9x104± 4.8x104 | 8.2x105 ± 5.6x105 | 3.6x105 ± 6.0x105 | X | X | |
|  | **ADULT ANAL FIN PAPILLAE (number per fish)** | | | | | | | | | | | | |
| F0 | 0 | 116±15 | 0 | 128±11 | 0 | 105±16 | 0 | 111±19 | 0 | 120±22 | 0 | 123±10 | |
| F1 | 0 | 83±21 | 0 | 111±9 | 0 | 111±20 | 0 | 100±25 | 0 | 66±44 | 0 | 0 | |
| F2 | 0 | 130±13 | 0 | 113±24 | 0 | 73±35 | 0 | 90±21 | 0 | 23±40 | 0 | 0 | |
|  | **SUBADULT ANAL FIN PAPILLAE (number per fish)** | | | | | | | | | | | | |
| F1 | 0 | 18±20 | 0 | 27±24 | 0 | 38±5 | 0 | 9±16 | 0 | 5±9 | 0 | 0 | |
| F2 | 0 | 35±27 | 0 | 19±24 | 0 | 13±22 | 0 | 13±19 | 0 | 6±17 | 0 | 0 | |

**Table S2.** The mean and standard deviation, if available, for each endpoint measured during medaka multi-generational test conducted at NIES at all nominal concentrations levels of 4tOP. “X” = no fish available; “-“ = measurement not in specific test design.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **4tOP NIES** | | | | | | | | | | | | | |
|  | **control** | | **6.25 μg/L** | | **12.5 μg/L** | | **25 μg/L** | | **50 μg/L** | | **100 μg/L** | | |
| **FECUNDITY (eggs per pair-day)** | | | | | | | | | | | | | |
| F0 | - | | - | | - | | - | | - | | - | | |
| F1 | 29 | | 34 | | 31 | | 33 | | 27 | | 6 | | |
| F2 | 27 | | 33 | | 25 | | 32 | | 32 | | X | | |
| **FERTILITY** | | | | | | | | | | | | | |
| F0 | - | | - | | - | | - | | - | | - | | |
| F1 | 99% | | 96% | | 98% | | 98% | | 80% | | 1% | | |
| F2 | 96% | | 99% | | 53% | | 86% | | 96% | | X | | |
| **HATCH** | | | | | | | | | | | | | |
| F1 | 92 ± 13% | | 89 ± 14% | | 91 ± 15% | | 86 ± 18% | | 88 ± 14% | | 89 ± 10% | | |
| F2 | 87 ± 19% | | 89 ± 15% | | 76 ± 15% | | 70 ± 24% | | 77 ± 112% | | X | | |
| **LARVAL SURVIVAL** | | | | | | | | | | | | | |
| F1 | - | | - | | - | | - | | - | | - | | |
| F2 | - | | - | | - | | - | | - | | - | | |
| **SUBADULT SURVIVAL** | | | | | | | | | | | | | |
| F1 | 100% | | 100% | | 100% | | 98% | | 96% | | 100% | | |
| F2 | 100% | | 100% | | 100% | | 100% | | 100% | | 100% | | |
| **ADULT WEIGHT (mg)** | | | | | | | | | | | | | |
| F0 | - | | - | | - | | - | | - | | - | | |
| F1 | - | | - | | - | | - | | - | | - | | |
| F2 | - | | - | | - | | - | | - | | - | | |
| **SUBADULT WEIGHT (mg)** | | | | | | | | | | | | | |
| F1 | 226 ± 27 | | 221 ± 33 | | 231 ± 28 | | 238 ± 30 | | 239 ± 30 | | 223 ± 5 | | |
| F2 | 200 ± 37 | | 208 ± 31 | | 208 ± 33 | | 233 ± 43 | | 224 ± 38 | | X | | |
| **ADULT LENGTH (mm)** | | | | | | | | | | | | | |
| F0 | - | | - | | - | | - | | - | | - | | |
| F1 | - | | - | | - | | - | | - | | - | | |
| F2 | - | | - | | - | | - | | - | | - | | |
| **SUBADULT LENGTH (mm)** | | | | | | | | | | | | | |
| F1 | 27 ± 1 | | 27 ± 1 | | 28 ± 1 | | 28 ± 1 | | 28 ± 1 | | 27 ± 2 | | |
| F2 | 27 ± 2 | | 27 ± 1 | | 27 ± 1 | | 28 ± 1 | | 27 ± 1 | | X | | |
|  | **control** | | **6.25 μg/L** | | **12.5 μg/L** | | **25 μg/L** | | **50 μg/L** | | **100 μg/L** | | |
|  | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | |
| **ADULT SURVIVAL** | | | | | | | | | | | | | |
| F0 | - | - | - | - | - | - | - | - | - | - | - | | - |
| F1 | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 83% | 33% | | 100% |
| F2 | 100% | 100% | 100% | 100% | 67% | 100% | 100% | 100% | 100% | 100% | X | | X |
| **ADULT VITELLOGENIN (ng per mg liver)** | | | | | | | | | | | | | |
| F0 | - | - | - | - | - | - | - | - | - | - | - | - | |
| F1 | - | - | - | - | - | - | - | - | - | - | - | - | |
| F2 | - | - | - | - | - | - | - | - | - | - | - | - | |
|  | **SUBADULT VITELLOGENIN (ng per mg liver)** | | | | | | | | | | | | |
| F1 | 490 | 2.3 | 720 | 4.8 | 840 | 9.4 | 1100 | 13 | 1300 | 50 | 1600 | 200 | |
| F2 | 470 | 2 | 950 | 8 | 700 | 12.5 | 1000 | 19 | 1300 | 33 | X | X | |
|  | **ADULT ANAL FIN PAPILLAE (number per fish)** | | | | | | | | | | | | |
| F0 | - | - | - | - | - | - | - | - | - | - | - | - | |
| F1 | 0 | 116±12 | 0 | 105±19 | 0 | 113±10 | 0 | 104±9 | 0 | 91±16 | 0 | 30±36 | |
| F2 | 0 | 120±20 | 0 | 95±36 | 0 | 103±27 | 0 | 104±12 | 0 | 85±13 | X | X | |
|  | **SUBADULT ANAL FIN PAPILLAE (number per fish)** | | | | | | | | | | | | |
| F1 | 0 | 71±13 | 0 | 10±9 | 0 | 23±10 | 0 | 15±18 | 0 | 12±16 | 0 | 1±6 | |
| F2 | 0 | 69±22 | 0 | 74±13 | 0 | 62±19 | 0 | 53±27 | 0 | 50±21 | X | X | |

**Table S3.** The mean and standard deviation for each endpoint measured during medaka multi-generational test conducted at CERI at all measured concentrations levels of 17β-estradiol. “X” = no fish available; “-“ = measurement not in specific test design.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **17β-Estradiol CERI** | | | | | | | | | | | | | |
|  | **control** | | **0.9 ng/L** | | **2.8 ng/L** | | **8.9 ng/L** | | **28 ng/L** | | **84 ng/L** | | |
| **FECUNDITY (eggs per pair-day)** | | | | | | | | | | | | | |
| F0 | 22.7 ± 2.6 | | 23.1 ± 2.7 | | 22.0 ± 4.6 | | 23.6± 2.2 | | 23.1 ± 2.3 | | 22.6 ± 3.3 | | |
| F1 | 26.7 ± 3.9 | | 28.5 ± 3.0 | | 23.5 ± 5.1 | | 25.8 ± 1.9 | | 18.6 ± 5.0 | | 6.8 ± 2.5 | | |
| F2 | 21.2 ± 4.6 | | 19.1 ± 9.4 | | 23.1 ± 2.9 | | 26.5 ± 3.5 | | 16.2 ± 9.7 | | X | | |
| **FERTILITY** | | | | | | | | | | | | | |
| F0 | 97 ± 4% | | 97 ± 5% | | 98 ± 3% | | 98 ± 2% | | 98 ± 2% | | 97 ± 4% | | |
| F1 | 97 ± 2% | | 84 ± 35% | | 99 ± 1% | | 79 ± 32% | | 34 ± 35% | | 11 ± 20% | | |
| F2 | 82 ± 24% | | 82 ± 39% | | 98 ± 1% | | 99 ± 1% | | 74 ± 17% | | X | | |
| **HATCH** | | | | | | | | | | | | | |
| F1 | 96 ± 6% | | 99 ± 1% | | 92 ± 3% | | 95 ± 3% | | 91 ± 5% | | 97 ± 2% | | |
| F2 | 96 ± 7% | | 85 ± 32% | | 97 ± 6% | | 85 ± 30% | | 53 ± 41 % | | X | | |
| **LARVAL SURVIVAL** | | | | | | | | | | | | | |
| F1 | - | | - | | - | | - | | - | | - | | |
| F2 | - | | - | | - | | - | | - | | - | | |
| **SUBADULT SURVIVAL** | | | | | | | | | | | | | |
| F1 | 100% | | 100% | | 100% | | 100% | | 98% | | 100% | | |
| F2 | 100% | | 100% | | 100% | | 100% | | 100% | | X | | |
| **ADULT WEIGHT (mg)** | | | | | | | | | | | | | |
| F0 | - | | - | | - | | - | | - | | - | | |
| F1 | - | | - | | - | | - | | - | | - | | |
| F2 | - | | - | | - | | - | | - | | - | | |
| **SUBADULT WEIGHT (mg)** | | | | | | | | | | | | | |
| F1 | 208 ± 27 | | 211 ± 38 | | 219 ± 38 | | 207 ± 44 | | 212 ± 36 | | 206 ± 28 | | |
| F2 | 208 ± 31 | | 216 ± 26 | | 224 ± 33 | | 215 ± 39 | | 227 ± 61 | | X | | |
| **ADULT LENGTH (mm)** | | | | | | | | | | | | | |
| F0 | - | | - | | - | | - | | - | | - | | |
| F1 | - | | - | | - | | - | | - | | - | | |
| F2 | - | | - | | - | | - | | - | | - | | |
| **SUBADULT LENGTH (mm)** | | | | | | | | | | | | | |
| F1 | 28 ± 1 | | 27 ± 1 | | 28 ± 1 | | 27 ± 2 | | 28 ± 1 | | 27 ± 1 | | |
| F2 | 27 ± 1 | | 28 ± 1 | | 28 ± 2 | | 28 ± 1 | | 28 ± 3 | | X | | |
|  | **control** | | **0.9 ng/L** | | **2.8 ng/L** | | **8.9 ng/L** | | **28 ng/L** | | **84 ng/L** | | |
|  | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | |
| **ADULT SURVIVAL** | | | | | | | | | | | | | |
| F0 | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | | 100% |
| F1 | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 83% | 100% | 83% | | 100% |
| F2 | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | X | | X |
| **ADULT VITELLOGENIN (ng per mg liver)** | | | | | | | | | | | | | |
| F0 | 800±91 | 1 ± 3 | 842±134 | 1 ± 1 | 1034±594 | 1 ± 1 | 861±160 | 2 ± 3 | 825±174 | 300±178 | 757±125 | 4152±882 | |
| F1 | 1271±135 | 1±1 | 3550±994 | 1±1 | 1101±132 | 1±1 | 1065±160 | 1±1 | 1054±201 | 88±86 | 1877±1544 | 3550±994 | |
| F2 | 1338±482 | 1±1 | 927±573 | 1±1 | 993±196 | 1±1 | 1081±293 | 1±1 | 1179±762 | 22±20 | X | X | |
|  | **SUBADULT VITELLOGENIN (ng per mg liver)** | | | | | | | | | | | | |
| F1 | 1193±627 | 1±3 | 1211±634 | 2±3 | 674±853 | 1±1 | 1255±1074 | 1±1 | 2157±1291 | 462±288 | 3990±  527 | 4039±  950 | |
| F2 | 975±208 | 1±1 | 1444±190 | 1±1 | 1000±585 | 1±1 | 2238±944 | 107±366 | 2217±1557 | 762±596 | X | X | |
|  | **ADULT ANAL FIN PAPILLAE (number per fish)** | | | | | | | | | | | | |
| F0 | 0 | 101±11 | 0 | 99±12 | 0 | 109±32 | 0 | 100±10 | 0 | 90±10 | 0 | 92±10 | |
| F1 | 0 | 117±9 | 0 | 108±9 | 0 | 120±12 | 0 | 91±5 | 0 | 75±8 | 0 | 0 | |
| F2 | 0 | 86±5 | 0 | 88±8 | 0 | 86±5 | 0 | 87±4 | 0 | 71±7 | X | X | |
|  | **SUBADULT ANAL FIN PAPILLAE (number per fish)** | | | | | | | | | | | | |
| F1 | 0 | 71±23 | 0 | 63±19 | 0 | 56±25 | 0 | 57±29 | 0 | 4±10 | 0 | 0 | |
| F2 | 0 | 67±4 | 0 | 73±3 | 0 | 62±4 | 0 | 60±4 | 0 | 22±5 | X | X | |

**Table S4.** The mean and standard deviation, if available, for each endpoint measured during medaka multi-generational test conducted at MED at all measured concentrations levels of CMP. “-“ = measurement not in specific test design.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **CMP MED** | | | | | | | | | | | | | |
|  | **control** | | **21 μg/L** | | **43 μg/L** | | **88 μg/L** | | **165 μg/L** | | **345 μg/L** | | |
| **FECUNDITY (eggs per pair-day)** | | | | | | | | | | | | | |
| F0 | 37.8 ± 6.9 | | 33.3 ± 10.6 | | 29.8 ± 15.7 | | 33.6 ± 5.3 | | 34.1 ± 2.2 | | 33.7 ± 8.4 | | |
| F1 | 32.5 ± 6.2 | | 38.9 ± 8.3 | | 23.9 ± 18.6 | | 31.2 ± 5.7 | | 35.9 ± 9.4 | | 34.3 ± 9.7 | | |
| F2 | 39.1 ± 6.8 | | 21.5 ± 15 | | 31.3 ± 11.2 | | 23.4 ± 16.4 | | 32.0 ± 7.6 | | 29.6 ± 5.1 | | |
| **FERTILITY** | | | | | | | | | | | | | |
| F0 | 86 ± 15% | | 95 ± 2% | | 74 ± 36% | | 91 ± 8% | | 86 ± 9% | | 89 ± 4% | | |
| F1 | 73 ± 34% | | 83 ± 21% | | 48 ± 42% | | 89 ± 5% | | 81 ± 26% | | 91 ± 9% | | |
| F2 | 92 ± 8% | | 47 ± 45% | | 67 ± 37% | | 54 ± 49% | | 82 ± 9% | | 88 ± 7% | | |
| **HATCH** | | | | | | | | | | | | | |
| F1 | 77 ± 17% | | 87 ± 14% | | 94 ± 5% | | 96 ± 2% | | 87 ± 13% | | 86 ± 16% | | |
| F2 | 68 ± 23% | | 81 ± 25% | | 79 ± 13% | | 94 ± 5% | | 90 ± 13% | | 95 ± 5% | | |
| **LARVAL SURVIVAL** | | | | | | | | | | | | | |
| F1 | - | | - | | - | | - | | - | | - | | |
| F2 | 65% | | 93% | | 94% | | 90% | | 68% | | 73% | | |
| **SUBADULT SURVIVAL** | | | | | | | | | | | | | |
| F1 | 98 ± 4% | | 100% | | 93 ± 5% | | 97 ± 5% | | 92 ± 4% | | 90 ± 5% | | |
| F2 | 95 ± 5% | | 97 ± 5% | | 97 ± 5% | | 95 ± 5% | | 98 ± 3% | | 92 ± 5% | | |
|  | | | | | | | | | | | | | |
|  | **control** | | **21 μg/L** | | **43 μg/L** | | **88 μg/L** | | **165 μg/L** | | **345 μg/L** | | |
|  | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | |
| **ADULT SURVIVAL** | | | | | | | | | | | | | |
| F0 | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | | 100% |
| F1 | 100% | 100% | 83% | 100% | 100% | 100% | 100% | 100% | 83% | 100% | 100% | | 100% |
| F2 | 100% | 100% | 67% | 100% | 100% | 100% | 100% | 83% | 100% | 100% | 100% | | 100% |
| **ADULT WEIGHT (mg)** | | | | | | | | | | | | | |
| F0 | 619±61 | 433±58 | 636±78 | 465±85 | 636±109 | 444±77 | 615±119 | 448±82 | 611±101 | 514±40 | 582±44 | 436±80 | |
| F1 | 604±76 | 467±129 | 646±190 | 429±115 | 865±271 | 405±78 | 576±230 | 418±124 | 740±120 | 499±110 | 686±126 | 389±59 | |
| F2 | 519±58 | 413±44 | 565±195 | 384±82 | 534±61 | 377±95 | 639±79 | 355±40 | 623±136 | 411±64 | 554±135 | 382±78 | |
| **SUBADULT WEIGHT (mg)** | | | | | | | | | | | | | |
| F1 | 243±99 | 210±59 | 236±58 | 204±55 | 225±51 | 177±31 | 198±46 | 195±35 | 197±57 | 185±47 | 211±59 | 182±37 | |
| F2 | 176±38 | 167±39 | 167±33 | 154±22 | 183±33 | 157±39 | 169±50 | 162±38 | 196±55 | 176±46 | 164±43 | 137±41 | |
| **ADULT LENGTH (mm)** | | | | | | | | | | | | | |
| F0 | 38±2 | 37±2 | 38±2 | 37±2 | 38±2 | 37±2 | 38±2 | 36±2 | 39±2 | 38±2 | 38±1 | 36±1 | |
| F1 | 38±2 | 37±3 | 37±2 | 35±5 | 39±2 | 36±2 | 37±3 | 33±5 | 38±2 | 36±1 | 37±1 | 34±1 | |
| F2 | 37±1 | 37±2 | 38±2 | 35±1 | 36±1 | 36±2 | 38±2 | 35±1 | 38±2 | 36±2 | 36±3 | 34±1 | |
| **SUBADULT LENGTH (mm)** | | | | | | | | | | | | | |
| F1 | 27±2 | 27±2 | 27±3 | 26±3 | 26±2 | 25±2 | 25±2 | 26±2 | 25±2 | 25±3 | 25±3 | 25±2 | |
| F2 | 26±1 | 25±2 | 25±1 | 25±1 | 25±1 | 25±2 | 25±2 | 25±2 | 26±2 | 25±2 | 24±2 | 24±3 | |
| **ADULT VITELLOGENIN (copies per ng total RNA)** | | | | | | | | | | | | | |
| F0 | 2.3x106 ± 1.4x106 | 2.9x104 ± 2.5x104 | 2.7x106 ± 2.1x106 | 6.7x104 ± 8.1x104 | 3.0x106 ± 1.8x106 | 3.3x104 ± 2.4x104 | 4.6x106 ± 8.5x105 | 3.2x104 ± 2.0x104 | 3.5x106 ± 7.7x105 | 1.6x104 ± 1.5x104 | 6.0x106 ± 1.4x106 | 5.7x104 ± 5.5x104 | |
| F1 | 9.2x106 ± 5.7x106 | 2.8x104 ± 4.6x104 | 1.2x107 ± 8.2x106 | 1.5x104 ± 1.5x104 | 1.9x107 ± 1.7x106 | 1.4x104 ± 1.3x104 | 3.5x107 ± 4.7x106 | 4.3x104 ± 8.7x104 | 2.0x107 ± 1.7x106 | 2.6x104 ± 3.1x104 | 2.1x107 ± 1.6x106 | 4.0x104 ± 3.1x104 | |
| F2 | 1.8x107 ± 9.6x106 | 8.2x104 ± 8.1x104 | 4.1x107 ± 7.1x107 | 2.5x103 ± 2.5x103 | 8.7x106 ± 3.9x106 | 1.4x105 ± 1.7x105 | 1.0x107 ± 1.4x107 | 3.5x105 ± 6.5x105 | 2.0x107 ± 2.1x106 | 2.4x105 ± 3.6x105 | 5.8x107 ± 8.4x106 | 1.5x105 ± 2.1x105 | |
|  | **SUBADULT VITELLOGENIN (copies per ng total RNA)** | | | | | | | | | | | | |
| F1 | 6.2x106 ± 3.9x106 | 3.1x104 ± 6.9x104 | 1.2x107 ± 3.9x107 | 3.7x104 ± 1.4x104 | 5.8x106 ± 5.3x106 | 8.2x104 ± 2.6x104 | 3.9x106 ± 5.0x106 | 1.2x104 ± 5.0x104 | 7.1x106 ± 7.2x106 | 3.8x104 ± 9.4x104 | 5.0x106 ± 2.5x106 | 4.1x104 ± 7.8x104 | |
| F2 | 1.4x107 ± 3.7x107 | 7.5x103 ± 1.2x104 | 3.8x107 ± 6.8x107 | 2.8x104 ± 5.8x104 | 8.1x107 ± 1.9x107 | 3.6x104 ± 6.9x104 | 1.8x107 ± 6.0x107 | 1.1x104 ± 1.6x104 | 2.5x106 ± 1.6x106 | 3.5x103 ± 5.4x103 | 3.5x106 ± 3.9x106 | 1.6x104 ± 5.8x104 | |
|  | **ADULT ANAL FIN PAPILLAE (number per fish)** | | | | | | | | | | | | |
| F0 | 0 | 138±31 | 0 | 145±22 | 0 | 121±22 | 0 | 134±17 | 0 | 150±42 | 0 | 138±20 | |
| F1 | 0 | 89±34 | 0 | 134±19 | 0 | 132±17 | 0 | 145±18 | 0 | 115±9 | 0 | 132±22 | |
| F2 | 0 | 122±22 | 0 | 110±35 | 0 | 105±15 | 0 | 114±28 | 0 | 124±29 | 0 | 122±22 | |
|  | **SUBADULT ANAL FIN PAPILLAE (number per fish)** | | | | | | | | | | | | |
| F1 | 0 | 89±32 | 0 | 94±26 | 0 | 88±18 | 0 | 95±28 | 0 | 85±30 | 0 | 84±20 | |
| F2 | 0 | 84±37 | 0 | 79±25 | 0 | 72±25 | 0 | 69±23 | 0 | 86±34 | 0 | 71±45 | |

**Table S5.** The mean and standard deviation for each endpoint measured during medaka multi-generational test conducted at CERI at all measured concentrations levels of DDT. “-“ = measurement not in specific test design.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **DDT CERI** | | | | | | | | | | | | |
|  | **control** | | **0.03 μg/L** | | **0.07 μg/L** | | **0.22 μg/L** | | **0.69 μg/L** | | **1.9 μg/L** | |
| **FECUNDITY (eggs per pair-day)** | | | | | | | | | | | | |
| F0 | 20.4 ± 2.9 | | 19.7 ± 7.8 | | 21.9 ± 1.4 | | 20.0 ± 3.1 | | 21.4 ± 2.3 | | 20.9 ± 1.6 | |
| F1 | 15.7 ± 9.3 | | 17.7 ± 8.1 | | 21.7 ± 11.1 | | 18.3 ± 4.5 | | 15.2 ± 7.8 | | 12.5 ± 10.9 | |
| F2 | 20.3 ± 6.8 | | 19.9 ± 4.1 | | 25.6 ± 3.6 | | 18.0 ± 5.4 | | 20.6 ± 1.3 | | 14.0 ± 6.1 | |
| **FERTILITY** | | | | | | | | | | | | |
| F0 | 92 ± 21% | | 99 ± 2% | | 98 ± 4% | | 96 ± 6% | | 97 ± 2% | | 97 ± 3% | |
| F1 | 95 ± 7% | | 96 ± 5% | | 99 ± 1% | | 92 ± 17% | | 81 ± 30% | | 46 ± 53% | |
| F2 | 86 ± 30% | | 99 ± 2% | | 94 ± 11% | | 73 ± 42% | | 99 ± 1% | | 39 ± 37% | |
| **HATCH** | | | | | | | | | | | | |
| F1 | 99 ± 2% | | 93 ± 20% | | 99 ± 4% | | 99 ± 2% | | 97 ± 5% | | 98 ± 3% | |
| F2 | 93 ± 12% | | 99 ± 2% | | 93 ± 11% | | 99 ± 2% | | 72 ± 40% | | 93 ± 8% | |
| **LARVAL SURVIVAL** | | | | | | | | | | | | |
| F1 | 100% | | 100% | | 97% | | 100% | | 100% | | 100% | |
| F2 | 100% | | 100% | | 100% | | 100% | | 100% | | 100% | |
| **SUBADULT SURVIVAL** | | | | | | | | | | | | |
| F1 | 100% | | 100% | | 100% | | 100% | | 100% | | 100% | |
| F2 | 100% | | 100% | | 98% | | 100% | | 100% | | 100% | |
| **ADULT SURVIVAL** | | | | | | | | | | | | |
| F0 | 100% | | 100% | | 83% | | 92% | | 100% | | 92% | |
| F1 | 100% | | 100% | | 100% | | 100% | | 100% | | 83% | |
| F2 | 100% | | 100% | | 100% | | 100% | | 100% | | 100% | |
| **SUBADULT WEIGHT (mg)** | | | | | | | | | | | | |
| F1 | 240 ± 33 | | 251 ± 34 | | 252 ± 41 | | 248 ± 36 | | 246 ± 42 | | 243 ± 35 | |
| F2 | 239 ± 33 | | 244 ± 36 | | 234 ± 43 | | 243 ± 39 | | 244 ± 33 | | 223 ± 37 | |
| **SUBADULT LENGTH (mm)** | | | | | | | | | | | | |
| F1 | 29 ± 1 | | 29 ± 1 | | 29 ± 1 | | 29 ± 1 | | 29 ± 1 | | 29 ± 2 | |
| F2 | 29 ± 1 | | 29 ± 1 | | 28 ± 1 | | 29 ± 1 | | 30 ± 1 | | 28 ± 1 | |
|  | **control** | | **0.03 μg/L** | | **0.07 μg/L** | | **0.22 μg/L** | | **0.69 μg/L** | | **1.9 μg/L** | |
|  | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** |
| **ADULT WEIGHT (mg)** | | | | | | | | | | | | |
| F0 | - | - | - | - | - | - | - | - | - | - | - | - |
| F1 | - | - | - | - | - | - | - | - | - | - | - | - |
| F2 | - | - | - | - | - | - | - | - | - | - | - | - |
| **ADULT LENGTH (mm)** | | | | | | | | | | | | |
| F0 | - | - | - | - | - | - | - | - | - | - | - | - |
| F1 | - | - | - | - | - | - | - | - | - | - | - | - |
| F2 | - | - | - | - | - | - | - | - | - | - | - | - |
| **ADULT VITELLOGENIN (ng per mg liver)** | | | | | | | | | | | | |
| F0 | 1238±561 | 3±6 | 1052±117 | ND | 991±77 | 3±3 | 1132±257 | 5±11 | 1385±494 | 8±8 | 1304±98 | 4738±261 |
| F1 | 1165±622 | ND | 1338±458 | ND | 1449±815 | ND | 1230±391 | ND | 1281±359 | 26±45 | 2354±1977 | 5261±1374 |
| F2 | 905±406 | ND | 944±106 | ND | 916±118 | 4±5 | 1520±870 | 3±2 | 1160±180 | 300±437 | 2058±278 | 6973±2212 |
|  | **SUBADULT VITELLOGENIN (ng per mg liver)** | | | | | | | | | | | |
| F1 | 628±682 | ND | 1001±693 | ND | 2489±1428 | 3±5 | 1299±913 | 1±1 | 3049±2453 | 243±840 | 5124±1223 | 1554±2725 |
| F2 | 750±815 | ND | 1022±707 | 1±1 | 1326±482 | 1±1 | 1531±513 | 1±1 | 1948±1086 | 1±1 | 5173±2032 | 7±8 |
|  | **ADULT ANAL FIN PAPILLAE (number per fish)** | | | | | | | | | | | |
| F0 | 0 | 98±15 | 0 | 98±6 | 0 | 89±16 | 0 | 87±14 | 0 | 94±20 | 0 | 86±20 |
| F1 | 0 | 53±27 | 0 | 66±16 | 0 | 64±18 | 0 | 54±24 | 0 | 49±27 | 0 | 19±21 |
| F2 | 0 | 86±17 | 0 | 114±14 | 0 | 98±13 | 0 | 93±14 | 0 | 87±15 | 0 | 76±10 |
|  | **SUBADULT ANAL FIN PAPILLAE (number per fish)** | | | | | | | | | | | |
| F1 | 0 | 53±27 | 0 | 66±16 | 0 | 64±18 | 0 | 54±24 | 0 | 49±27 | 0 | 10±4 |
| F2 | 0 | 56±17 | 0 | 65±17 | 0 | 66±16 | 0 | 68±19 | 0 | 57±21 | 0 | 21±4 |

**Table S6.** The mean and standard deviation for each endpoint measured during medaka multi-generational test conducted at NIES at all nominal concentration levels of tamoxifen. “-“ = measurement not in specific test design.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Tamoxifen NIES** | | | | | | | | | | | | |
|  | **control** | | **1.3 μg/L** | | **2.5 μg/L** | | **5 μg/L** | | **10 μg/L** | | **20 μg/L** | |
| **FECUNDITY (eggs per pair-day)** | | | | | | | | | | | | |
| F0 | - | | - | | - | | - | | - | | - | |
| F1 | 23.1 ± 8.3 | | 23.6 ± 7.2 | | 24.6 ± 7.5 | | 25.3 ± 9.6 | | 23.2 ± 11.4 | | 7.7 ± 8.8 | |
| F2 | - | | - | | - | | - | | - | | - | |
| **FERTILITY** | | | | | | | | | | | | |
| F0 | - | | - | | - | | - | | - | | - | |
| F1 | 98 ± 2% | | 96 ± 5% | | 98 ± 2% | | 96 ± 4% | | 93 ± 10% | | 85 ± 13% | |
| F2 | - | | - | | - | | - | | - | | - | |
| **HATCH** | | | | | | | | | | | | |
| F1 | 95 ± 5% | | 94 ± 6% | | 88 ± 16% | | 85 ± 14% | | 80 ± 30% | | 72 ± 21% | |
| F2 | 85 ± 14% | | 75 ± 19% | | 64 ± 20% | | 64 ± 28% | | 58 ± 25% | | 69 ± 26% | |
| **LARVAL SURVIVAL** | | | | | | | | | | | | |
| F1 | - | | - | | - | | - | | - | | - | |
| F2 | - | | - | | - | | - | | - | | - | |
| **SUBADULT SURVIVAL** | | | | | | | | | | | | |
| F1 | - | | - | | - | | - | | - | | - | |
| F2 | - | | - | | - | | - | | - | | - | |
| **ADULT SURVIVAL** | | | | | | | | | | | | |
| F0 | - | | - | | - | | - | | - | | - | |
| F1 | 100% | | 100% | | 100% | | 100% | | 100% | | 100% | |
| F2 | - | | - | | - | | - | | - | | - | |
| **ADULT WEIGHT (mg)** | | | | | | | | | | | | |
| F0 | - | | - | | - | | - | | - | | - | |
| F1 | - | | - | | - | | - | | - | | - | |
| F2 | - | | - | | - | | - | | - | | - | |
| **ADULT LENGTH (mm)** | | | | | | | | | | | | |
| F0 | - | | - | | - | | - | | - | | - | |
| F1 | - | | - | | - | | - | | - | | - | |
| F2 | - | | - | | - | | - | | - | | - | |
|  | **control** | | **1.3 μg/L** | | **2.5 μg/L** | | **5 μg/L** | | **10 μg/L** | | **20 μg/L** | |
|  | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** |
| **SUBADULT WEIGHT (mg)** | | | | | | | | | | | | |
| F1 | 129±23 | 128±23 | 126±19 | 126±21 | 115±20 | 128±20 | 142±27 | 141±25 | 117±19 | 115±32 | 95±42 | 85±29 |
| F2 | 240±31 | 212±32 | 230±31 | 210±28 | 224±48 | 197±39 | 245±67 | 241±43 | 226±68 | 207±45 | 194±38 | 200±37 |
| **SUBADULT LENGTH (mm)** | | | | | | | | | | | | |
| F1 | 23±1 | 23±1 | 23±1 | 23±2 | 22±2 | 24±1 | 24±1 | 24±1 | 23±1 | 22±1 | 21±3 | 19±1 |
| F2 | 28±1 | 27±1 | 27±1 | 27±1 | 27±2 | 26±2 | 27±2 | 28±2 | 27±3 | 27±2 | 26±1 | 26±1 |
| **ADULT VITELLOGENIN (ng per mg liver)** | | | | | | | | | | | | |
| F0 | - | - | - | - | - | - | - | - | - | - | - | - |
| F1 | 766±194 | 63±14 | 724±137 | 25±20 | 688±120 | 55±25 | 405±337 | 46±29 | 574±78 | 66±28 | 515±226 | 64±14 |
| F2 | - | - | - | - | - | - | - | - | - | - | - | - |
|  | **SUBADULT VITELLOGENIN (ng per mg liver)** | | | | | | | | | | | |
| F1 | 34±79 | ND | 32±85 | 2±4 | 16±16 | 5±5 | 55±92 | 15±18 | 23±17 | 8±10 | 27±38 | 14±5 |
| F2 | 1362±742 | ND | 568±413 | 2±2 | 383±320 | 8±5 | 803±629 | 13±11 | 283±307 | 24±25 | 99±59 | 23±13 |
|  | **ADULT ANAL FIN PAPILLAE (number per fish)** | | | | | | | | | | | |
| F0 | - | - | - | - | - | - | - | - | - | - | - | - |
| F1 | 0 | 106±10 | 0 | 113±22 | 0 | 115±35 | 0 | 151±19 | 0 | 136±27 | 0 | 140±4 |
| F2 | - | - | - | - | - | - | - | - | - | - | - | - |
|  | **SUBADULT ANAL FIN PAPILLAE (number per fish)** | | | | | | | | | | | |
| F1 | 1±3 | 15±17 | 2±8 | 5±8 | 2±7 | 6±9 | 2±8 | 15±18 | 4±11 | 11±16 | 1±5 | 2±8 |
| F2 | 0 | 80±20 | 0 | 51±23 | 0 | 47±22 | 0 | 75±31 | 0 | 52±25 | 0 | 27±17 |

**Table S7.** The mean and standard deviation, when available, for each endpoint measured during medaka multi-generational test conducted at MED at all measured concentrations levels of trenbolone. “X” = no fish available; “-“ = measurement not in specific test design.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Trenbolone MED** | | | | | | | | | | | | | |
|  | **control** | | **2 ng/L** | | **5 ng/L** | | **13 ng/L** | | **32 ng/L** | | **84 ng/L** | | |
| **FECUNDITY (eggs per pair-day)** | | | | | | | | | | | | | |
| F0 | 18.1 ± 6.0 | | 23.1 ± 8.1 | | 22.6 ± 5.5 | | 20.7 ± 4.5 | | 22.0 ± 6.6 | | 11.6 ± 5.5 | | |
| F1 | 24.9 ± 12.4 | | 20.8 ± 8.2 | | 25.2 ± 6.8 | | 11.4 ± 12.3 | | 0 | | 0 | | |
| F2 | 23.5 ± 4.8 | | 27.2 ± 7.3 | | 22.7 ± 6.8 | | 24.0 ± 4.6 | | X | | X | | |
| **FERTILITY** | | | | | | | | | | | | | |
| F0 | 88 ± 5% | | 89 ± 8% | | 93 ± 5% | | 93 ± 6% | | 90 ± 5% | | 87 ± 6% | | |
| F1 | 97 ± 3% | | 46 ± 33% | | 85 ± 15% | | 46 ± 37% | | X | | X | | |
| F2 | 84 ± 14% | | 87 ± 14% | | 60 ± 14% | | 86 ± 2% | | X | | X | | |
| **HATCH** | | | | | | | | | | | | | |
| F1 | 80 ± 17% | | 72 ± 29% | | 80 ± 21% | | 87 ± 28% | | 83 ± 15% | | 81 ± 14% | | |
| F2 | 87 ± 17% | | 80 ± 18% | | 79 ± 31% | | 97 ± 3% | | X | | X | | |
| **LARVAL SURVIVAL** | | | | | | | | | | | | | |
| F1 | - | | - | | - | | - | | - | | - | | |
| F2 | - | | - | | - | | - | | - | | - | | |
| **SUBADULT SURVIVAL** | | | | | | | | | | | | | |
| F1 | 96 ± 5% | | 97 ± 8% | | 98 ± 4% | | 95 ± 8% | | 81 ± 16% | | 88 ± 8% | | |
| F2 | 95 ± 5% | | 85 ± 6% | | 96 ± 5% | | 100% | | X | | X | | |
|  | | | | | | | | | | | | | |
|  | **control** | | **2 ng/L** | | **5 ng/L** | | **13 ng/L** | | **32 ng/L** | | **84 ng/L** | | |
|  | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | |
| **ADULT SURVIVAL** | | | | | | | | | | | | | |
| F0 | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | | 100% |
| F1 | 83% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | | 100% |
| F2 | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | | 100% |
| **ADULT WEIGHT (mg)** | | | | | | | | | | | | | |
| F0 | 535 ± 65 | 464 ±74 | 559 ±55 | 484±103 | 535±76 | 434 ±24 | 545 ±58 | 439 ±59 | 549 ± 60 | 432 ±41 | 672 ±88 | 475 ±32 | |
| F1 | 499±150 | 367±36 | 586±123 | 439±85 | 499 ± 78 | 398±88 | 627±216 | 428±68 | 783±241 | 490±48 | 432±14 | 412±57 | |
| F2 | 562±106 | 383±47 | 512±130 | 444±68 | 598±75 | 357±25 | 576±77 | 418±56 | X | X | X | X | |
| **SUBADULT WEIGHT (mg)** | | | | | | | | | | | | | |
| F1 | 213±56 | 186±46 | 167±45 | 188±41 | 197±48 | 191±44 | 199±53 | 187±42 | 170±58 | 154±49 | 167±47 | 168±27 | |
| F2 | 208±41 | 182±43 | 210±60 | 202±44 | 201±62 | 171±49 | 228±41 | **208**±42 | X | X | X | X | |
| **ADULT LENGTH (mm)** | | | | | | | | | | | | | |
| F0 | 38±1 | 37±1 | 38±1 | 37±1 | 37±1 | 36±1 | 37±1 | 37±1 | 37±1 | 36±1 | 38±1 | 37±1 | |
| F1 | 35±2 | 33±2 | 36±3 | 36±2 | 35±1 | 35±2 | 38±3 | 35±1 | 38±1 | 37±1 | 35±1 | 35±1 | |
| F2 | 34±2 | 35±1 | 37±1 | 36±1 | 36±2 | 34±2 | 38±2 | 34±1 | X | X | X | X | |
| **SUBADULT LENGTH (mm)** | | | | | | | | | | | | | |
| F1 | 26±2 | 26±2 | 26±2 | 25±1 | 26±2 | 26±1 | 27±2 | 26±1 | 27±3 | 25±2 | 25±2 | 25±2 | |
| F2 | 25±2 | 26±3 | 27±3 | 27±2 | 26±3 | 24±4 | 27±2 | 27±3 | X | X | X | X | |
| **ADULT VITELLOGENIN (copies per ng total RNA)** | | | | | | | | | | | | | |
| F0 | 7.8x106± 6.8x106 | 8.1x104 ± 1.8x104 | 1.6x107 ± 1.8x107 | 3.8x104 ± 7.8x104 | 5.1x106 ± 2.2x106 | 8.1x104 ± 1.8x104 | 1.6x105 ± 2.2x105 | 3.6x104± 2.4x104 | 1.4x107 ± 2.7x107 | 1.4x104 ± 1.4x104 | 3.1x106± 1.2x106 | 6.3x103 ± 4.7x103 | |
| F1 | 1.6x106 ± 1.0x106 | 2.9x104 ± 3.8x104 | 2.2x106 ± 1.2x106 | 6.6x103 ± 5.2x103 | 4.0x106 ± 1.2x106 | 1.4x104 ± 1.1x104 | 1.8x106 ± 1.3x106 | 4.8x103± 4.9x103 | 2.7x106 ± 2.8x106 | 3.2x103 ± 3.1x103 | 9.9x102± 4.4x102 | 8.0x102 ± 7.0x102 | |
| F2 | 3.4x106 ± 9.0x105 | 3.3x104 ± 2.1x104 | 3.7x106 ± 7.4x105 | 1.7x104 ± 1.2x104 | 5.1x106 ± 3.5x106 | 8.1x103 ± 2.6x103 | 2.7x106 ± 1.5x106 | 4.4x104± 8.2x104 | X | X | X | X | |
|  | **SUBADULT VITELLOGENIN (copies per ng total RNA)** | | | | | | | | | | | | |
| F1 | 1.7x106 ± 3.2x106 | 6.8x103 ± 1.3x104 | 1.6x106 ± 1.6x106 | 3.9x103 ± 6.4x104 | 2.3x106 ± 1.3x106 | 1.3x104 ± 2.1x104 | 1.3x106 ± 1.4x106 | 9.5x103± 2.0x104 | 6.4x105 ± 1.3x106 | 1.8x103 ± 1.7x103 | 4.7x103± 1.2x104 | 1.6x103 ± 1.1x103 | |
| F2 | 3.4x106 ± 9.0x105 | 3.3x104 ± 2.1x104 | 3.7x106 ± 7.4x105 | 1.7x104 ± 1.2x104 | 5.1x106 ± 3.5x106 | 8.1x103 ± 2.6x103 | 2.7x106 ± 1.5x106 | 4.4x104± 8.2x104 | X | X | X | X | |
|  | **ADULT ANAL FIN PAPILLAE (number per fish)** | | | | | | | | | | | | |
| F0 | 0 | 111±18 | 0 | 113±11 | 0 | 122±18 | 0 | 113±20 | 16 ± 24 | 106±16 | 64 ± 17 | 115±22 | |
| F1 | 23±52 | 133±11 | 0 | 117±50 | 0 | 124±22 | 23±46 | 135±14 | 39±46 | 131±17 | 114±24 | 120±18 | |
| F2 | 0 | 133±7 | 0 | 140±17 | 0 | 142±24 | 0 | 127±22 | X | X | X | X | |
|  | **SUBADULT ANAL FIN PAPILLAE (number per fish)** | | | | | | | | | | | | |
| F1 | 0 | 85±26 | 0 | 71±33 | 0 | 99±23 | 0 | 80±22 | 39±42 | 100±23 | 78±20 | 83±21 | |
| F2 | 0 | 95±30 | 0 | 116±32 | 0 | 99±39 | 0 | 88±18 | X | X | X | X | |

**Table S8.** The mean and standard deviation for each endpoint measured during medaka multi-generational test conducted at MED at all measured concentrations levels of vinclozolin. “X” = no fish available; “-“ = measurement not in specific test design.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Vinclozolin MED** | | | | | | | | | | | | | |
|  | **control** | | **17 μg/L** | | **33 μg/L** | | **70 μg/L** | | **136 μg/L** | | **253 μg/L** | | |
| **FECUNDITY (eggs per pair-day)** | | | | | | | | | | | | | |
| F0 | 23.7±8.7 | | 14.8±7.1 | | 14.0±6.8 | | 16.7±5.3 | | 16.0±8.2 | | 6.6±2.3 | | |
| F1 | 25.0±3.1 | | 25.8±4.3 | | 19.9±8.6 | | 29.0 | | 26.4±9.7 | | 0.6 | | |
| F2 | - | | - | | - | | - | | - | | - | | |
| **FERTILITY** | | | | | | | | | | | | | |
| F0 | 85±13% | | 73±32% | | 88±8% | | 85±10% | | 76±38% | | 68±20% | | |
| F1 | 93±7% | | 89±7% | | 65±32% | | 87% | | 89±7% | | 0% | | |
| F2 | - | | - | | - | | - | | - | | - | | |
| **HATCH** | | | | | | | | | | | | | |
| F1 | 97±7% | | 76±27% | | 89±17% | | 83±22% | | 94±10% | | 67±58% | | |
| F2 | 83±15% | | 88±13% | | 91±11% | | 87±5% | | 95±5% | | X | | |
| **LARVAL SURVIVAL** | | | | | | | | | | | | | |
| F1 | 84±10% | | 82±10% | | 73±11% | | 68±13% | | 56±11% | | 25±21% | | |
| F2 | 74±14% | | 83±9% | | 66±18% | | 52±15% | | 68±10% | | X | | |
| **SUBADULT SURVIVAL** | | | | | | | | | | | | | |
| F1 | 100% | | 100% | | 99% | | 100% | | 100% | | 100% | | |
| F2 | 100% | | 100% | | 99% | | 100% | | 100% | | X | | |
|  | | | | | | | | | | | | | |
|  | **control** | | **17 μg/L** | | **33 μg/L** | | **70 μg/L** | | **136 μg/L** | | **253 μg/L** | | |
|  | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | |
| **ADULT SURVIVAL** | | | | | | | | | | | | | |
| F0 | 100% | 100% | 100% | 100% | 100% | 100% | 83% | 100% | 83% | 100% | 100% | | 100% |
| F1 | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | | 100% |
| F2 | - | - | - | - | - | - | - | - | - | - | - | | - |
| **ADULT WEIGHT (mg)** | | | | | | | | | | | | | |
| F0 | 380±117 | 275±13 | 391±46 | 305±49 | 372±38 | 337±35 | 423±71 | 336±46 | 399±112 | 322±49 | 516±113 | 361±54 | |
| F1 | 312±50 | 257±26 | 367±66 | 294±41 | 361±40 | 292±34 | 476±129 | 350 | 439±75 | 300±43 | 492±29 | X | |
| F2 | - | - | - | - | - | - | - | - | - | - | - | - | |
| **SUBADULT WEIGHT (mg)** | | | | | | | | | | | | | |
| F1 | 194±38 | 159±12 | 175±55 | 160±34 | 203±49 | 151±32 | 197±65 | X | 186±51 | 154 | 187±25 | X | |
| F2 | 152±30 | 134±32 | 181±30 | 143±19 | 182±29 | 144±20 | 154±35 | X | 181±37 | 151±34 | X | X | |
| **ADULT LENGTH (mm)** | | | | | | | | | | | | | |
| F0 | 34±2 | 33±1 | 34±2 | 34±1 | 34±1 | 33±1 | 35±1 | 34±1 | 35±2 | 34±1 | 36±3 | 34±2 | |
| F1 | 32±1 | 32±1 | 34±1 | 33±1 | 34±1 | 33±1 | 35±1 | 35 | 36±2 | 34±2 | 35±0 | X | |
| F2 | - | - | - | - | - | - | - | - | - | - | - | - | |
| **SUBADULT LENGTH (mm)** | | | | | | | | | | | | | |
| F1 | 26±1 | 25±1 | 25±2 | 25±2 | 26±2 | 24±2 | 25±3 | X | 26±2 | 25 | 25±2 | X | |
| F2 | 25±2 | 24±3 | 26±1 | 25±1 | 26±2 | 25±1 | 25±2 | X | 26±1 | 25±2 | X | X | |
| **ADULT VITELLOGENIN (copies per ng total RNA)** | | | | | | | | | | | | | |
| F0 | - | - | - | - | - | - | - | - | - | - | - | - | |
| F1 | - | - | - | - | - | - | - | - | - | - | - | - | |
| F2 | - | - | - | - | - | - | - | - | - | - | - | - | |
|  | **SUBADULT VITELLOGENIN (copies per ng total RNA)** | | | | | | | | | | | | |
| F1 | 8.2x105± 8.5x105 | 660±  680 | 2.7x105± 2.8x105 | 2030±  1760 | 6.0x105 ± 2.2x105 | 410±  710 | 9.1x105 ± 1.9x106 | X | 5.8x105 ± 6.0x105 | 270±  270 | 8.5x105 ± 3.2x105 | X | |
| F2 | 4.2x105 ± 4.6x105 | 1600±  5000 | 4.1x105 ± 4.1x105 | 1800±  6300 | 5.7x105 ± 5.1x105 | 1100±  1600 | 3.4x105 ± 4.5x105 | X | 6.2x105 ± 6.9x105 | 4200±  12000 | X | X | |
|  | **ADULT ANAL FIN PAPILLAE (number per fish)** | | | | | | | | | | | | |
| F0 | 0 | 95±17 | 0 | 77±25 | 25±38 | 68±40 | 6±12 | 120±30 | 20±45 | 80±46 | 0 | 111±35 | |
| F1 | 0 | 21±30 | 0 | 60±19 | 0 | 48±21 | 14±46 | 102 | 8±22 | 44±33 | 0 | X | |
| F2 | - | - | - | - | - | - | - | - | - | - | - | - | |
|  | **SUBADULT ANAL FIN PAPILLAE (number per fish)** | | | | | | | | | | | | |
| F1 | 7±22 | 78±24 | 2±10 | 57±23 | 2±10 | 37±42 | 0 | X | 5±13 | 27 | 0 | X | |
| F2 | 9±26 | 55±30 | 2±9 | 44±14 | 2±8 | 28±19 | 2±10 | X | 3±11 | 21±18 | X | X | |

**Table S9.** The mean and standard deviation for each endpoint measured during medaka multi-generational test conducted at MED at all measured concentrations levels of prochloraz. “X” = no fish available; “-“ = measurement not in specific test design.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Prochloraz MED** | | | | | | | | | | | | | |
|  | **control** | | **5 μg/L** | | **9 μg/L** | | **17 μg/L** | | **25 μg/L** | | **41 μg/L** | | |
| **FECUNDITY (eggs per pair-day)** | | | | | | | | | | | | | |
| F0 | 32.9±4.3 | | 31.0±12.2 | | 24.6±14.7 | | 31.1±10.0 | | 22.6±13.4 | | 11.7±12.4 | | |
| F1 | 17.4±17.4 | | 20.9±13.8 | | 25.7±13.8 | | 8.0±7.0 | | 10.0±9.9 | | X | | |
| F2 | 33.0±4.8 | | 23.2±12.2 | | 24.0±16.5 | | 23.0±5.9 | | 8.7±11.0 | | X | | |
| **FERTILITY** | | | | | | | | | | | | | |
| F0 | 79±39% | | 78±38% | | 86±19% | | 93±3% | | 85±10% | | 82±7% | | |
| F1 | 92±3% | | 89±10% | | 85±21% | | 90±14% | | 57±38% | | X | | |
| F2 | 91±9% | | 84±7% | | 93±8% | | 88±16% | | 45±29% | | X | | |
| **HATCH** | | | | | | | | | | | | | |
| F1 | 85±11% | | 93±6% | | 96±2% | | 85±9% | | 65±23% | | 27±1% | | |
| F2 | 94±4% | | 82±35% | | 92±1% | | 87±37% | | 91% | | X | | |
| **LARVAL SURVIVAL** | | | | | | | | | | | | | |
| F1 | 76% | | 63% | | 69% | | 52% | | 34% | | 13% | | |
| F2 | 77% | | 73% | | 68% | | 100% | | 45% | | X | | |
| **SUBADULT SURVIVAL** | | | | | | | | | | | | | |
| F1 | 100% | | 100% | | 100% | | 100% | | 100% | | X | | |
| F2 | 97% | | 100% | | 97% | | 95% | | 95% | | X | | |
|  | | | | | | | | | | | | | |
|  | **control** | | **5 μg/L** | | **9 μg/L** | | **17 μg/L** | | **25 μg/L** | | **41 μg/L** | | |
|  | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | **XX** | **XY** | |
| **ADULT SURVIVAL** | | | | | | | | | | | | | |
| F0 | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | | 100% |
| F1 | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 83±26% | 92±20% | X | | X |
| F2 | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 88±26% | X | | X |
| **ADULT WEIGHT (mg)** | | | | | | | | | | | | | |
| F0 | 556±56 | 444±61 | 566±76 | 461±53 | 592±39 | 478±79 | 594±83 | 473±88 | 601±57 | 457±84 | 679±186 | 540±83 | |
| F1 | 630±150 | 567±30 | 523±82 | 508±39 | 657±132 | 430±91 | 600±60 | 525±60 | 522±34 | 522±83 | X | X | |
| F2 | 602±89 | 609±59 | 744±193 | 599±128 | 798±245 | 594±57 | 667±104 | 556±48 | 623±171 | 512±51 | X | X | |
| **SUBADULT WEIGHT (mg)** | | | | | | | | | | | | | |
| F1 | 222±26 | 195±24 | 204±32 | 205±16 | 164±40 | 148±25 | 181±41 | 155±37 | 148±34 | 146±17 | X | X | |
| F2 | 249±51 | 213±53 | 215±58 | 189±32 | 163±42 | 164±33 | 155±40 | 158±32 | X | X | X | X | |
| **ADULT LENGTH (mm)** | | | | | | | | | | | | | |
| F0 | 37±1 | 37±1 | 38±1 | 37±2 | 39±1 | 37±1 | 39±1 | 37±2 | 39±2 | 37±1 | 39±1 | 38±2 | |
| F1 | 41±4 | 37±2 | 37±3 | 36±2 | 38±2 | 34±3 | 39±2 | 36±1 | 36±3 | 34±2 | X | X | |
| F2 | 37±2 | 37±1 | 38±3 | 37±3 | 40±1 | 37±3 | 39±1 | 36±1 | 37±5 | 36±1 | X | X | |
| **SUBADULT LENGTH (mm)** | | | | | | | | | | | | | |
| F1 | 27±1 | 26±1 | 26±2 | 27±2 | 24±2 | 24±2 | 25±2 | 24±3 | 24±3 | 23±2 | X | X | |
| F2 | 28±1 | 26±2 | 27±2 | 27±1 | 25±2 | 25±1 | 27±6 | 27±5 | X | X | X | X | |
| **ADULT VITELLOGENIN (copies per ng total RNA)** | | | | | | | | | | | | | |
| F0 | - | - | - | - | - | - | - | - | - | - | - | - | |
| F1 | - | - | - | - | - | - | - | - | - | - | - | - | |
| F2 | - | - | - | - | - | - | - | - | - | - | - | - | |
|  | **SUBADULT VITELLOGENIN (copies per ng total RNA)** | | | | | | | | | | | | |
| F1 | 6.6x106 ± 4.2x106 | 4.5x103± 1.3x104 | 2.9x106 ± 2.8x106 | 980 ±  510 | 8.6x105 ± 1.1x106 | 8.6x103± 2.6x104 | 4.3x105 ± 3.5x105 | 1.1x104± 4.1x104 | 1.4x105 ± 2.1x105 | 840±  560 | X | X | |
| F2 | 4.3x106 ± 2.4x106 | 4.0x103± 5.3x103 | 2.7x106 ± 2.1x106 | 2.4x103 ± 2.9x103 | 1.9x106 ± 1.9x106 | 1.7x103± 1.4x103 | 3.9x105 ± 8.1x105 | 9.4x103± 2.1x104 | X | X | X | X | |
|  | **ADULT ANAL FIN PAPILLAE (number per fish)** | | | | | | | | | | | | |
| F0 | 0 | 97±27 | 0 | 105±26 | 0 | 94±23 | 0 | 104±15 | 0 | 112±19 | 0 | 98±20 | |
| F1 | 0 | 99±22 | 19±47 | 111±16 | 0 | 96±34 | 15±36 | 84±10 | 0 | 96±25 | X | X | |
| F2 | 0 | 95±14 | 0 | 95±9 | 0 | 107±16 | 0 | 98±11 | 0 | 93±12 | X | X | |
|  | **SUBADULT ANAL FIN PAPILLAE (number per fish)** | | | | | | | | | | | | |
| F1 | 0 | 74±24 | 0 | 70±14 | 2±8 | 35±23 | 0 | 49±24 | 0 | 54±29 | X | X | |
| F2 | 0 | 55±22 | 0 | 59±19 | 0 | 54±23 | 0 | 34±34 | X | X | X | X | |