

Two-generation reproductive toxicity study in rats with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (SR05241)

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Table 1 General appearance in F0 and F1 parental male rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Gener- ation | Item | Pre-mating period | | | | Breeding period | | | |
|--------------------------------------|--|-------------------|------------|-----|------|-----------------|------------|-----|------|
| | | Control | DCBS (ppm) | | | Control | DCBS (ppm) | | |
| | | | 80 | 600 | 4500 | | 80 | 600 | 4500 |
| F0 | Number of animals examined | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 |
| | Number of animals with abnormal findings | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 |
| | Findings ^a | | | | | | | | |
| | Deformation of the face | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | Malocclusion | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 |
| | Salivation | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | Soil of periocular fur/perinasal fur | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 |
| Abdominal distention | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | |
| F1 | Number of animals examined | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 |
| | Number of animals with abnormal findings | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | Findings ^a | | | | | | | | |
| | Malocclusion | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| Soil of periocular fur/perinasal fur | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | |

a: Values represent the number of animals that showed abnormal findings during each period.

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Table 2 General appearance in F0 and F1 parental female rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Gener- ation | Item | Breeding period | | | | | | | | | | | |
|-----------------|---|-------------------|------------|----|-----|-------------------------------|------------|--------|-----|-------------------------------|------------|--------|----|
| | | Pre-mating period | | | | Gestation period ^a | | | | Lactation period ^b | | | |
| | | Control | DCBS (ppm) | | | Control | DCBS (ppm) | | | Control | DCBS (ppm) | | |
| 80 | 600 | | 4500 | 80 | 600 | | 4500 | 80 | 600 | | 4500 | | |
| F0 | Number of animals examined ^c | 24 | 24 | 24 | 24 | 22 (2) | 24 | 24 | 24 | 22 (2) | 24 | 24 | 24 |
| | Number of animals with abnormal findings ^c | 0 | 0 | 0 | 0 | 0 (0) | 0 | 1 | 2 | 5 (0) | 0 * | 1 | 1 |
| | Findings ^{c,d} | | | | | | | | | | | | |
| | Malocclusion | 0 | 0 | 0 | 0 | 0 (0) | 0 | 0 | 0 | 2 (0) | 0 | 0 | 0 |
| | Crushing of incisors | 0 | 0 | 0 | 0 | 0 (0) | 0 | 0 | 0 | 1 (0) | 0 | 0 | 0 |
| | Soil of periorcular fur/perinasal fur | 0 | 0 | 0 | 0 | 0 (0) | 0 | 0 | 0 | 3 (0) | 0 | 0 | 0 |
| | Subcutaneous mass | 0 | 0 | 0 | 0 | 0 (0) | 0 | 0 | 0 | 2 (0) | 0 | 0 | 0 |
| | Alopecia | 0 | 0 | 0 | 0 | 0 (0) | 0 | 1 | 2 | 0 (0) | 0 | 1 | 1 |
| F1 | Number of animals examined ^c | 24 | 24 | 24 | 24 | 23 (1) | 22 (2) | 21 (3) | 24 | 23 (1) | 22 (2) | 21 (3) | 24 |
| | Number of animals with abnormal findings ^c | 0 | 0 | 0 | 0 | 0 (0) | 0 (0) | 0 (0) | 1 | 1 (0) | 0 (0) | 0 (0) | 3 |
| | Findings ^{c,d} | | | | | | | | | | | | |
| | Malocclusion | 0 | 0 | 0 | 0 | 0 (0) | 0 (0) | 0 (0) | 1 | 0 (0) | 0 (0) | 0 (0) | 3 |
| | Soil of periorcular fur/perinasal fur | 0 | 0 | 0 | 0 | 0 (0) | 0 (0) | 0 (0) | 0 | 0 (0) | 0 (0) | 0 (0) | 2 |
| | Soil of perigenital fur | 0 | 0 | 0 | 0 | 0 (0) | 0 (0) | 0 (0) | 0 | 0 (0) | 0 (0) | 0 (0) | 1 |
| | Found dead | 0 | 0 | 0 | 0 | 0 (0) | 0 (0) | 0 (0) | 0 | 1 (0) | 0 (0) | 0 (0) | 0 |

Statistical analyses were made based on the total number of animals examined.

a: Including the mating period and delivery.

b: Including the period from weaning to autopsy.

c: Values in parentheses represent the number of animals that were non-pregnant and that did not produce viable pups.

d: Values represent the number of animals that showed abnormal findings during each period.

*: Significantly different from the control at $p \leq 0.05$ by Fisher's exact probability test.

Table 3 Body weights of F0 and F1 parental male rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Gener- ation | Group | Number of animals | | Pre-mating period | | | | | | | | | | Breeding period | | | | Autopsy day | | | |
|-----------------|---------------|-------------------------|------|-----------------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|-----------------|----------|----------|---------------------|----------------|--------------------|-------|--|
| | | | | Body weight (g) in treatment week | | | | | | | | | | | | | | | | | |
| | | | | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | | | |
| F0 | Control | 24 | Mean | 155.6 | 227.5 | 293.5 | 351.3 | 395.7 | 433.9 | 466.4 | 494.6 | 518.4 | 538.9 | 556.9 | 566.4 | 583.0 | 598.4 | 611.1 | 624.4 | | |
| | | | S.D. | 4.7 | 8.4 | 15.5 | 22.9 | 28.7 | 33.9 | 40.1 | 45.3 | 49.6 | 54.4 | 59.1 | 60.0 | 64.1 | 67.6 | 70.3 | 76.0 | | |
| | DCBS 80 ppm | 24 | Mean | 155.9 | 224.8 | 287.7 | 343.3 | 384.3 | 418.3 | 450.6 | 478.4 | 500.2 | 521.0 | 539.2 | 550.1 | 567.0 | 584.0 | 598.4 | 612.5 | | |
| | | | S.D. | 4.6 | 7.5 | 12.1 | 20.3 | 24.9 | 30.7 | 35.6 | 41.4 | 44.3 | 47.0 | 48.8 | 49.7 | 53.7 | 56.5 | 59.0 | 61.0 | | |
| | DCBS 600 ppm | 24 | Mean | 155.6 | 225.9 | 288.7 | 345.2 | 388.6 | 424.6 | 456.8 | 481.5 | 502.5 | 521.0 | 538.8 | 548.3 | 564.6 | 579.5 | 592.0 | 603.4 | | |
| | | | S.D. | 4.6 | 9.0 | 14.2 | 20.0 | 25.2 | 29.4 | 35.3 | 39.0 | 42.1 | 42.8 | 46.1 | 44.9 | 45.9 | 46.6 | 48.3 | 51.2 | | |
| | DCBS 4500 ppm | 24 | Mean | 155.7 | 215.4 ** | 274.4 ** | 327.9 ** | 368.8 ** | 403.3 ** | 434.0 ** | 457.0 ** | 477.2 ** | 496.2 ** | 512.6 ** | 522.5 ** | 537.8 ** | 550.8 ^{SS} | 564.5 * | 575.4 ^S | | |
| | | | S.D. | 4.5 | 6.2 | 10.5 | 16.0 | 21.0 | 25.5 | 27.3 | 28.5 | 30.9 | 32.4 | 36.0 | 35.8 | 38.0 | 37.8 | 41.1 | 42.3 | | |
| | F1 | Control | 24 | Mean | 71.8 | 124.0 | 189.8 | 253.8 | 320.2 | 379.4 | 426.4 | 463.9 | 498.2 | 528.8 | 553.3 | 565.1 | 583.2 | 601.4 | 615.3 | 630.7 | |
| | | | | S.D. | 6.4 | 10.6 | 13.7 | 15.1 | 18.6 | 23.5 | 30.5 | 37.2 | 44.3 | 49.2 | 54.0 | 55.9 | 62.4 | 67.5 | 68.0 | 74.7 | |
| | | DCBS 80 ppm | 24 | Mean | 71.6 | 123.6 | 187.0 | 251.9 | 315.1 | 371.2 | 416.8 | 451.4 | 482.5 | 509.3 | 533.3 | 542.4 | 559.0 | 575.8 | 589.8 | 605.1 | |
| | | | | S.D. | 6.4 | 9.7 | 13.6 | 17.0 | 20.7 | 23.3 | 27.8 | 29.7 | 32.7 | 36.4 | 39.8 | 38.8 | 42.2 | 43.8 | 44.5 | 47.7 | |
| DCBS 600 ppm | | 24 | Mean | 71.8 | 125.6 | 191.8 | 253.3 | 316.5 | 372.4 | 416.0 | 451.5 | 485.1 | 515.7 | 540.3 | 552.3 | 570.0 | 586.9 | 598.9 | 614.2 | | |
| | | | S.D. | 7.7 | 12.4 | 15.2 | 17.7 | 20.9 | 23.5 | 26.7 | 32.5 | 37.4 | 40.9 | 44.3 | 45.3 | 48.8 | 49.3 | 52.7 | 52.5 | | |
| DCBS 4500 ppm | | 24 | Mean | 67.2 | 119.6 | 183.8 | 246.7 | 311.0 | 368.6 | 416.7 | 453.2 | 487.7 | 515.1 | 540.9 | 552.0 | 572.6 | 590.5 | 604.3 | 622.6 | | |
| | | | S.D. | 7.9 | 12.9 | 18.6 | 22.9 | 27.3 | 29.4 | 31.3 | 35.5 | 37.3 | 40.8 | 41.9 | 45.7 | 48.1 | 49.7 | 50.8 | 51.8 | | |

Values in parentheses are the number of animals examined.

*: Significantly different from the control at $p \leq 0.05$ by Dunnett's test.

** : Significantly different from the control at $p \leq 0.01$ by Dunnett's test.

^S: Significantly different from the control at $p \leq 0.05$ by Mann-Whitney U-test.

^{SS}: Significantly different from the control at $p \leq 0.01$ by Mann-Whitney U-test.

Table 4 Body weights of F0 and F1 parental female rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Gener- ation | Group | Number of animals | Pre-mating period | | | | | | | | | | | Breeding period | | | | | | | | | | | |
|-----------------|---------------|-------------------------|-------------------|-------|---------------------|-------|-------|-------|-------|-------|-------|-------|-------|-----------------|-------|--------------------|--------------------|--------------------|---------------------|---------------------|---------------------|---------------------|--------------------|--------------------|------|
| | | | Treatment week | | | | | | | | | | | Gestation day | | | | Lactation day | | | Autopsy day | | | | |
| | | | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 0 | 7 | 14 | 20 | 0 | 4 | 7 | | 14 | 21 | | |
| F0 | Control | 24 | Mean | 121.1 | 154.5 | 172.1 | 194.5 | 211.8 | 226.8 | 239.7 | 253.5 | 261.9 | 266.1 | 272.2 | (22) | (22) | (22) | (22) | (22) | (22) | (22) | (22) | (22) | (22) | |
| | | | S.D. | 4.0 | 8.3 | 12.8 | 15.9 | 19.9 | 22.7 | 25.0 | 26.9 | 27.8 | 29.1 | 30.6 | 272.0 | 307.7 | 342.9 | 414.0 | 325.0 | 334.1 | 333.7 | 338.0 | 315.4 | 305.9 | |
| | DCBS 80 ppm | 24 | Mean | 121.3 | 157.3 | 180.1 | 202.5 | 221.7 | 237.7 | 252.0 | 265.4 | 274.4 | 279.8 | 285.8 | 287.8 | 324.1 | 355.2 | 420.8 | 329.9 | 340.7 | 343.3 | 348.5 | 323.5 | 311.6 | |
| | | | S.D. | 3.9 | 8.1 | 12.7 | 15.9 | 17.3 | 20.2 | 23.0 | 23.2 | 23.1 | 22.8 | 25.6 | 23.4 | 25.8 | 27.3 | 29.4 | 24.4 | 20.1 | 20.0 | 19.0 | 17.1 | 17.1 | |
| | DCBS 600 ppm | 24 | Mean | 121.0 | 155.6 | 178.1 | 199.7 | 218.2 | 235.5 | 250.8 | 263.5 | 271.5 | 276.3 | 284.5 | 286.5 | 326.8 [§] | 360.2 | 429.4 | 334.1 | 343.2 | 345.1 | 349.9 | 322.5 | 313.7 | |
| | | | S.D. | 3.8 | 7.5 | 11.5 | 15.0 | 16.4 | 17.3 | 18.9 | 21.3 | 20.7 | 21.5 | 23.2 | 22.3 | 21.3 | 23.7 | 25.4 | 19.1 | 21.9 | 21.5 | 18.2 | 17.6 | 17.8 | |
| | DCBS 4500 ppm | 24 | Mean | 121.0 | 147.6 ^{**} | 166.5 | 185.9 | 204.5 | 219.2 | 232.4 | 244.4 | 249.8 | 256.6 | 262.4 | 262.4 | 293.3 [§] | 323.9 [*] | 389.4 [*] | 298.4 ^{§§} | 303.6 ^{§§} | 310.6 ^{§§} | 316.3 ^{§§} | 301.3 [§] | 288.5 [§] | |
| | | | S.D. | 3.9 | 6.5 | 9.1 | 11.8 | 12.8 | 16.9 | 16.2 | 17.1 | 17.8 | 18.9 | 17.9 | 17.7 | 18.7 | 18.6 | 21.6 | 19.4 | 15.7 | 15.3 | 14.9 | 13.9 | 16.2 | |
| | F1 | Control | 24 | Mean | 67.7 | 109.9 | 150.2 | 179.3 | 207.2 | 231.7 | 252.1 | 264.9 | 282.5 | 291.8 | 301.3 | (23) | (23) | (23) | (23) | (23) | (23) | (22) | (22) | (22) | (22) |
| | | | | S.D. | 6.1 | 9.6 | 13.2 | 14.5 | 18.4 | 22.6 | 25.8 | 29.2 | 30.3 | 34.0 | 36.2 | 33.7 | 36.8 | 41.9 | 51.4 | 42.4 | 37.0 | 35.2 | 36.0 | 33.2 | 32.5 |
| | | DCBS 80 ppm | 24 | Mean | 67.7 | 109.4 | 151.2 | 183.7 | 210.8 | 234.1 | 255.3 | 269.5 | 285.3 | 292.8 | 301.7 | (22) | (22) | (22) | (22) | (22) | (22) | (22) | (22) | (22) | (22) |
| | | | | S.D. | 6.1 | 8.0 | 9.9 | 13.4 | 18.3 | 21.9 | 26.1 | 27.7 | 29.4 | 33.0 | 34.2 | 34.0 | 37.5 | 40.3 | 45.8 | 43.9 | 40.9 | 38.1 | 27.3 | 26.3 | 28.5 |
| DCBS 600 ppm | | 24 | Mean | 67.7 | 109.0 | 150.6 | 182.2 | 207.3 | 232.1 | 252.7 | 269.6 | 283.6 | 294.2 | 304.7 | (22) | (22) | (22) | (22) | (21) | (21) | (21) | (21) | (21) | (21) | |
| | | | S.D. | 7.2 | 10.5 | 11.8 | 13.0 | 15.9 | 20.2 | 21.1 | 22.7 | 24.2 | 26.5 | 26.2 | 24.8 | 26.9 | 25.5 | 32.5 | 27.7 | 22.3 | 22.7 | 24.1 | 23.9 | 23.1 | |
| DCBS 4500 ppm | | 24 | Mean | 64.3 | 108.7 | 151.5 | 179.5 | 206.5 | 230.6 | 251.6 | 268.1 | 281.3 | 291.4 | 301.7 | (22) | (22) | (22) | (22) | (21) | (21) | (21) | (21) | (21) | (21) | |
| | | | S.D. | 7.5 | 9.2 | 10.5 | 12.1 | 13.6 | 16.0 | 20.4 | 21.8 | 22.6 | 25.3 | 27.8 | 27.1 | 28.5 | 32.0 | 36.1 | 36.2 | 34.7 | 34.8 | 37.0 | 33.1 | 30.8 | |

Values in parentheses are the number of animals examined.

*: Significantly different from the control at $p \leq 0.05$ by Dunnett's test.

** : Significantly different from the control at $p \leq 0.01$ by Dunnett's test.

§: Significantly different from the control at $p \leq 0.05$ by Mann-Whitney U-test.

§§: Significantly different from the control at $p \leq 0.01$ by Mann-Whitney U-test.

Table 5 Body weight gains of F0 and F1 parental male rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Gener- ation | Group | Number of animals | | Pre-mating period | | | | | | | | | | Breeding period | | | | 0-Autopsy day | |
|-----------------|---------------|-------------------------|------|---|----------|----------|----------|----------|----------|----------|----------|----------|----------|-----------------|---------------|---------------------|---------------------|--------------------|-------|
| | | | | Body weight gain (g) in treatment weeks | | | | | | | | | | | | | | | |
| | | | | 0-1 | 0-2 | 0-3 | 0-4 | 0-5 | 0-6 | 0-7 | 0-8 | 0-9 | 0-10 | 0-11 | 0-12 | 0-13 | 0-14 | | |
| F0 | Control | 24 | Mean | 71.9 | 137.8 | 195.6 | 240.0 | 278.3 | 310.8 | 339.0 | 362.8 | 383.3 | 401.3 | 410.8 | 427.4 | 442.8 | 455.5 | 468.8 | |
| | | | S.D. | 6.0 | 13.4 | 21.1 | 26.9 | 32.2 | 38.4 | 43.6 | 48.0 | 52.7 | 57.4 | 58.2 | 62.3 | 65.8 | 68.4 | 74.1 | |
| | DCBS 80 ppm | 24 | Mean | 69.0 | 131.8 | 187.4 | 228.5 | 262.4 | 294.8 | 322.5 | 344.3 | 365.1 | 383.3 | (23) 394.0 | (23) 411.0 | (23) 428.0 | (23) 442.4 | (23) 456.4 | |
| | | | S.D. | 4.2 | 9.3 | 17.9 | 22.8 | 28.7 | 33.7 | 39.5 | 42.4 | 44.9 | 46.7 | 47.5 | 51.4 | 54.4 | 57.0 | 59.0 | |
| | DCBS 600 ppm | 24 | Mean | 70.3 | 133.1 | 189.6 | 233.0 | 269.0 | 301.2 | 326.0 | 347.0 | 365.5 | 383.3 | 392.7 | 409.0 | 424.0 | 436.4 | 447.8 | |
| | | | S.D. | 5.7 | 11.3 | 17.9 | 23.0 | 27.2 | 33.0 | 36.7 | 39.7 | 40.4 | 43.7 | 42.5 | 43.4 | 44.0 | 45.8 | 48.8 | |
| | DCBS 4500 ppm | 24 | Mean | 59.7 ** | 118.7 ** | 172.2 ** | 213.1 ** | 247.5 ** | 278.3 ** | 301.3 ** | 321.5 ** | 340.5 ** | 356.9 ** | 366.8 ** | 382.0 ** | 395.1 ^{ss} | 408.8 ^{ss} | 419.7 ^s | |
| | | | S.D. | 3.8 | 7.7 | 13.1 | 18.7 | 23.2 | 25.4 | 26.8 | 29.0 | 30.5 | 34.0 | 33.9 | 35.9 | 35.9 | 39.3 | 40.4 | |
| | F1 | Control | 24 | Mean | 52.3 | 118.0 | 182.0 | 248.4 | 307.7 | 354.7 | 392.2 | 426.4 | 457.1 | 481.6 | 493.3 | 511.4 | 529.7 | 543.6 | 558.9 |
| | | | | S.D. | 5.7 | 9.6 | 12.2 | 17.0 | 23.6 | 30.9 | 38.1 | 45.3 | 50.2 | 55.2 | 57.0 | 63.6 | 68.6 | 69.1 | 75.9 |
| | | DCBS 80 ppm | 24 | Mean | 52.0 | 115.4 | 180.3 | 243.5 | 299.6 | 345.3 | 379.8 | 411.0 | 437.8 | 461.8 | 470.8 | 487.4 | 504.3 | 518.2 | 533.5 |
| | | | | S.D. | 4.5 | 9.0 | 13.3 | 18.0 | 21.6 | 27.1 | 29.1 | 32.1 | 36.2 | 39.3 | 38.8 | 42.6 | 43.9 | 44.4 | 48.1 |
| DCBS 600 ppm | | 24 | Mean | 53.8 | 120.0 | 181.5 | 244.7 | 300.6 | 344.3 | 379.7 | 413.3 | 443.9 | 468.5 | 480.5 | 498.2 | 515.1 | 527.1 | 542.4 | |
| | | | S.D. | 5.3 | 9.3 | 13.4 | 17.3 | 21.5 | 25.5 | 31.2 | 36.1 | 39.9 | 43.3 | 44.4 | 48.3 | 48.6 | 52.2 | 52.3 | |
| DCBS 4500 ppm | | 24 | Mean | 52.5 | 116.6 | 179.5 | 243.8 | 301.5 | 349.5 | 386.0 | 420.5 | 447.9 | 473.7 | 484.8 | 505.4 | 523.3 | 537.2 | 555.4 | |
| | | | S.D. | 5.8 | 12.1 | 16.5 | 21.2 | 23.7 | 25.9 | 30.4 | 32.7 | 36.3 | 37.8 | 41.5 | 43.7 | 45.5 | 46.7 | 48.2 | |

Values in parentheses are the number of animals examined.

** : Significantly different from the control at $p \leq 0.01$ by Dunnett's test.

^s : Significantly different from the control at $p \leq 0.05$ by Mann-Whitney U-test.

^{ss} : Significantly different from the control at $p \leq 0.01$ by Mann-Whitney U-test.

Table 6 Body weight gains of F0 and F1 parental female rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Gener- ation | Group | Number of animals | Pre-mating period | | | | | | | | | | | Breeding period | | | | | | | | |
|-----------------|-------------|-------------------------|----------------------|------|--------|-------|-------|-------|-------|-------|-------|-------|--------|-----------------|---------------------|-------|----------------|------|-------|--------------------|------------------|------|
| | | | Body weight gain (g) | | | | | | | | | | | Gestation days | | | Lactation days | | | | 0-Autopsy day | |
| | | | Treatment weeks | | | | | | | | | | | 0-7 | 0-14 | 0-20 | 0-4 | 0-7 | 0-14 | 0-21 | | |
| | | | 0-1 | 0-2 | 0-3 | 0-4 | 0-5 | 0-6 | 0-7 | 0-8 | 0-9 | 0-10 | | | | | | | | | | |
| F0 | Control | 24 | Mean | 33.5 | 51.0 | 73.4 | 90.7 | 105.8 | 118.6 | 132.5 | 140.8 | 145.0 | 151.1 | (22) | (22) | (22) | (22) | (22) | (22) | (22) | (22) | (22) |
| | | | S.D. | 6.4 | 11.0 | 13.9 | 17.8 | 20.7 | 22.7 | 24.6 | 25.7 | 26.9 | 28.4 | 7.7 | 11.2 | 19.3 | 10.6 | 17.8 | 17.7 | 15.9 | 26.4 | |
| | DCBS 80 ppm | 24 | Mean | 36.0 | 58.9 * | 81.3 | 100.5 | 116.4 | 130.7 | 144.1 | 153.1 | 158.5 | 164.6 | 36.3 | 67.4 | 133.0 | 10.8 | 13.4 | 18.5 | -6.4 | 190.3 | |
| | | | S.D. | 6.0 | 10.7 | 13.8 | 15.5 | 18.5 | 21.3 | 21.5 | 21.6 | 21.3 | 24.0 | 6.1 | 9.1 | 11.4 | 8.8 | 11.0 | 13.2 | 12.6 | 15.5 | |
| DCBS 600 ppm | 24 | Mean | 34.6 | 57.0 | 78.7 | 97.1 | 114.4 | 129.8 | 142.5 | 150.5 | 155.2 | 163.5 | 40.4 * | 73.7 | 143.0 | 9.1 | 11.0 | 15.8 | -11.5 | 192.7 | | |
| | | S.D. | 5.9 | 10.3 | 13.7 | 15.6 | 16.6 | 18.4 | 20.7 | 20.2 | 21.0 | 22.9 | 5.4 | 9.6 | 12.7 | 10.7 | 9.2 | 9.4 | 10.5 | 17.0 | | |
| DCBS 4500 ppm | 24 | Mean | 26.6 ** | 45.5 | 64.9 | 83.5 | 98.2 | 111.4 | 123.4 | 128.8 | 135.6 | 141.4 | 30.9 * | 61.5 ** | 127.0 ^{§§} | 5.2 | 12.2 | 17.9 | 2.8 * | 167.5 [§] | | |
| | | S.D. | 5.6 | 8.1 | 10.4 | 11.8 | 15.9 | 15.2 | 15.5 | 16.5 | 17.8 | 16.9 | 5.1 | 6.2 | 12.3 | 10.2 | 13.7 | 14.3 | 18.0 | 14.5 | | |
| F1 | Control | 24 | Mean | 42.3 | 82.5 | 111.6 | 139.5 | 164.0 | 184.5 | 197.3 | 214.8 | 224.2 | 233.6 | (23) | (23) | (23) | (23) | (22) | (22) | (22) | (22) | (22) |
| | | | S.D. | 4.2 | 9.4 | 11.8 | 15.6 | 19.8 | 23.5 | 26.9 | 27.8 | 31.6 | 34.1 | 7.6 | 12.3 | 26.8 | 9.8 | 15.0 | 17.9 | 21.1 | 30.3 | |
| | DCBS 80 ppm | 24 | Mean | 41.7 | 83.5 | 116.0 | 143.1 | 166.4 | 187.5 | 201.8 | 217.6 | 225.0 | 234.0 | (22) | (22) | (22) | (22) | (22) | (22) | (22) | (22) | (22) |
| | | | S.D. | 3.3 | 6.7 | 12.0 | 16.5 | 20.4 | 24.5 | 26.1 | 28.4 | 32.0 | 33.2 | 6.2 | 11.0 | 20.1 | 11.8 | 13.4 | 22.7 | 28.5 | 27.3 | |
| DCBS 600 ppm | 24 | Mean | 41.3 | 82.9 | 114.5 | 139.5 | 164.4 | 185.0 | 201.9 | 215.9 | 226.5 | 237.0 | (22) | (22) | (22) | (21) | (21) | (21) | (21) | (21) | (21) | |
| | | S.D. | 5.7 | 8.2 | 10.9 | 13.3 | 17.7 | 18.8 | 21.2 | 22.7 | 25.0 | 24.9 | 6.4 | 9.9 | 21.9 | 11.3 | 12.6 | 19.0 | 16.7 | 20.9 | | |
| DCBS 4500 ppm | 24 | Mean | 44.4 | 87.3 | 115.3 | 142.3 | 166.3 | 187.3 | 203.8 | 217.0 | 227.1 | 237.4 | (22) | (22) | (22) | (21) | (21) | (21) | (21) | (21) | (21) | |
| | | S.D. | 4.1 | 7.9 | 12.4 | 12.9 | 16.2 | 20.8 | 21.9 | 23.2 | 26.4 | 29.0 | 9.0 | 11.5 | 17.7 | 11.9 | 17.2 | 27.0 | 32.1 | 31.1 | | |

Values in parentheses are the number of animals examined.

*: Significantly different from the control at $p \leq 0.05$ by Dunnett's test.

** : Significantly different from the control at $p \leq 0.01$ by Dunnett's test.

§: Significantly different from the control at $p \leq 0.05$ by Mann-Whitney U-test.

§§: Significantly different from the control at $p \leq 0.01$ by Mann-Whitney U-test.

Table 7 Food consumption of F0 and F1 parental male rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Gener- ation | Group | Number of animals | | Pre-mating period | | | | | | | | | | Breeding period | | | |
|-----------------|---------------|-------------------------|------|--|---------|---------|---------|---------|---------|--------|---------|------|------|-----------------|---------|---------|------|
| | | | | Food consumption (g/day) in treatment week | | | | | | | | | | 12 | 13 | 14 | |
| | | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | | | | |
| F0 | Control | 24 | Mean | 22.9 | 27.2 | 28.4 | 29.0 | 29.2 | 29.6 | 29.4 | 29.7 | 29.6 | 29.3 | 28.5 | 29.2 | 29.3 | |
| | | | S.D. | 1.1 | 1.9 | 2.5 | 2.7 | 2.7 | 2.7 | 2.6 | 2.8 | 3.0 | 2.9 | 2.7 | 2.8 | 2.8 | |
| | DCBS 80 ppm | 24 | Mean | 22.5 | 26.6 | 27.5 | 27.9 | 28.1 | 28.8 | 28.7 | 28.7 | 29.1 | 29.1 | 28.3 | 28.6 | 28.6 | |
| | | | S.D. | 0.9 | 1.6 | 2.4 | 2.4 | 2.5 | 2.8 | 2.9 | 2.6 | 2.8 | 2.5 | 2.7 | 3.0 | 2.9 | |
| | DCBS 600 ppm | 24 | Mean | 22.6 | 26.5 | 28.0 | 28.3 | 28.6 | 28.7 | 28.4 | 28.1 | 28.5 | 28.5 | 27.9 | 27.7 | 28.0 | |
| | | | S.D. | 1.3 | 1.7 | 2.1 | 2.3 | 2.3 | 2.4 | 2.3 | 2.5 | 2.4 | 2.5 | 2.2 | 2.0 | 2.2 | |
| | DCBS 4500 ppm | 24 | Mean | 21.2 ** | 24.3 ** | 25.8 ** | 26.5 ** | 26.8 ** | 27.5 * | 27.4 * | 27.3 ** | 27.7 | 27.7 | 27.1 | 26.9 ** | 27.1 ** | |
| | | | S.D. | 0.9 | 1.6 | 1.9 | 1.9 | 2.0 | 1.8 | 1.8 | 2.1 | 2.3 | 2.1 | 2.0 | 1.9 | 2.2 | |
| | F1 | Control | 24 | Mean | 14.2 | 20.9 | 25.2 | 28.9 | 30.6 | 31.4 | 31.3 | 31.1 | 31.0 | 30.4 | 29.7 | 29.7 | 29.8 |
| | | | | S.D. | 1.3 | 1.8 | 2.0 | 2.0 | 2.3 | 3.0 | 3.1 | 3.0 | 2.7 | 2.8 | 2.8 | 2.8 | 2.8 |
| | | DCBS 80 ppm | 24 | Mean | 14.7 | 20.8 | 24.8 | 27.4 * | 29.0 * | 29.6 * | 29.6 * | 29.6 | 29.8 | 30.0 | 28.9 | 28.2 | 28.6 |
| | | | | S.D. | 1.1 | 1.6 | 1.7 | 1.9 | 1.9 | 2.2 | 2.0 | 1.8 | 1.9 | 2.1 | 2.3 | 2.3 | 1.8 |
| DCBS 600 ppm | | 24 | Mean | 14.8 | 21.4 | 25.0 | 27.5 | 29.2 | 29.3 ** | 29.8 | 30.0 | 29.9 | 29.9 | 29.0 | 29.2 | 28.8 | |
| | | | S.D. | 1.3 | 1.3 | 1.2 | 1.6 | 1.9 | 1.9 | 2.2 | 2.2 | 2.1 | 2.0 | 2.1 | 1.9 | 2.3 | |
| DCBS 4500 ppm | | 24 | Mean | 14.2 | 20.5 | 24.6 | 27.1 * | 29.1 | 29.8 | 29.8 | 30.0 | 29.8 | 29.9 | 29.8 | 28.8 | 29.4 | |
| | | | S.D. | 1.4 | 2.2 | 2.4 | 2.7 | 2.5 | 2.0 | 2.2 | 2.4 | 2.3 | 2.3 | 3.3 | 2.9 | 2.8 | |

Values in parentheses are the number of animals examined.

*: Significantly different from the control at $p \leq 0.05$ by Dunnett's test.

**: Significantly different from the control at $p \leq 0.01$ by Dunnett's test.

Table 8 Food consumption of F0 and F1 parental female rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Gener- ation | Group | Number of animals | Pre-mating period | | | | | | | | | | | Breeding period | | | | | | |
|-----------------|---------------|-------------------------|--------------------------|---------|------|------|------|------|------|------|------|------|------|-----------------|------|-------|----------------|------|-------------------|------|
| | | | Food consumption (g/day) | | | | | | | | | | | Gestation days | | | Lactation days | | | |
| | | | Treatment week | | | | | | | | | | | 0-7 | 7-14 | 14-20 | 0-7 | 7-14 | 14-21 | |
| | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | | | | | | | | |
| F0 | Control | 24 | Mean | 16.3 | 16.9 | 17.7 | 18.0 | 18.2 | 18.7 | 18.8 | 18.5 | 18.0 | 17.8 | (22) | (22) | (22) | (22) | (22) | (22) | |
| | | | S.D. | 1.0 | 1.5 | 1.6 | 1.7 | 1.9 | 1.9 | 2.0 | 2.0 | 1.7 | 1.9 | 2.4 | 2.5 | 2.0 | 4.8 | 7.2 | 8.1 | |
| | DCBS 80 ppm | 24 | Mean | 16.4 | 17.8 | 18.2 | 18.6 | 18.6 | 19.3 | 19.5 | 18.8 | 18.5 | 18.2 | 21.5 | 23.4 | 22.8 | 34.2 | 50.3 | 65.9 | |
| | | | S.D. | 1.0 | 1.5 | 1.7 | 1.6 | 2.0 | 1.8 | 1.6 | 1.5 | 1.7 | 1.7 | 2.1 | 2.0 | 2.0 | 3.3 | 4.1 | 4.4 | |
| | DCBS 600 ppm | 24 | Mean | 16.2 | 17.6 | 17.8 | 18.5 | 18.7 | 19.3 | 19.2 | 18.9 | 18.8 | 18.7 | 22.7 | 24.8 | 23.7 | 33.9 | 50.2 | 65.0 | |
| | | | S.D. | 0.9 | 1.2 | 1.3 | 1.5 | 1.7 | 1.6 | 1.8 | 1.7 | 1.9 | 1.8 | 1.9 | 2.7 | 2.0 | 4.5 | 5.1 | 5.5 | |
| | DCBS 4500 ppm | 24 | Mean | 15.1 ** | 16.2 | 16.6 | 17.6 | 17.9 | 18.1 | 18.3 | 17.9 | 17.7 | 17.9 | 20.5 | 22.7 | 23.0 | 31.7 | 47.9 | 63.1 [§] | |
| | | | S.D. | 1.0 | 1.6 | 1.5 | 1.4 | 1.6 | 1.5 | 1.7 | 1.5 | 1.6 | 1.5 | 1.9 | 1.8 | 1.5 | 3.7 | 3.8 | 5.4 | |
| | F1 | Control | 24 | Mean | 13.0 | 17.5 | 18.9 | 20.1 | 20.8 | 20.9 | 21.3 | 21.1 | 20.4 | 20.7 | (23) | (23) | (23) | (22) | (22) | (22) |
| | | | | S.D. | 1.1 | 1.6 | 1.7 | 1.8 | 2.3 | 2.3 | 2.8 | 2.3 | 2.6 | 2.3 | 2.2 | 3.3 | 3.6 | 4.3 | 5.5 | 6.7 |
| | | DCBS 80 ppm | 24 | Mean | 13.5 | 17.5 | 19.0 | 19.9 | 20.6 | 21.2 | 21.0 | 20.9 | 20.3 | 20.7 | (22) | (22) | (22) | (22) | (22) | (22) |
| | | | | S.D. | 0.9 | 1.4 | 1.6 | 1.7 | 1.9 | 2.3 | 2.1 | 2.2 | 2.1 | 1.9 | 2.4 | 3.1 | 3.0 | 5.5 | 8.2 | 9.4 |
| DCBS 600 ppm | | 24 | Mean | 13.2 | 17.6 | 18.9 | 19.4 | 20.5 | 20.6 | 20.8 | 21.1 | 20.4 | 21.0 | (22) | (22) | (22) | (21) | (21) | (21) | |
| | | | S.D. | 1.2 | 1.5 | 1.7 | 1.9 | 2.1 | 2.2 | 2.3 | 2.1 | 1.7 | 1.9 | 2.3 | 1.9 | 1.9 | 5.4 | 8.4 | 10.0 | |
| DCBS 4500 ppm | | 24 | Mean | 13.0 | 17.7 | 19.1 | 19.8 | 20.7 | 21.1 | 21.0 | 21.0 | 20.7 | 21.1 | 23.8 | 25.6 | 25.5 | (23) | (23) | (23) | |
| | | | S.D. | 1.2 | 1.4 | 1.5 | 1.8 | 1.7 | 2.1 | 1.9 | 1.9 | 1.8 | 2.0 | 2.5 | 3.3 | 2.6 | 5.2 | 6.4 | 8.7 | |

Values in parentheses are the number of animals examined.
 **: Significantly different from the control at $p \leq 0.01$ by Dunnett's test.
 §: Significantly different from the control at $p \leq 0.05$ by Mann-Whitney U-test.

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Table 9 Test substance intake of F0 and F1 parental male rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Gener- ation | Group | Number of animals | Pre-mating period | | | | | | | | | | Breeding period | | | All the periods | | | |
|-----------------|---------------|-------------------------|---|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----------------|-----|-----|-----------------|---|-----|------|
| | | | Test substance intake (mg/kg/day) in treatment week | | | | | | | | | | 12 | 13 | 14 | Min | - | Max | Mean |
| | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | | | | | | | |
| F0 | DCBS 80 ppm | 24 | 8.0 | 7.4 | 6.4 | 5.8 | 5.4 | 5.1 | 4.8 | 4.6 | 4.5 | 4.3 | 4.0 | 3.9 | 3.8 | 3.8 | - | 8.0 | 5.2 |
| | DCBS 600 ppm | 24 | 60 | 55 | 49 | 44 | 40 | 38 | 35 | 34 | 33 | 32 | 30 | 29 | 28 | 28 | - | 60 | 39 |
| | DCBS 4500 ppm | 24 | 443 | 399 | 354 | 323 | 299 | 285 | 270 | 257 | 251 | 243 | 227 | 220 | 216 | 216 | - | 443 | 291 |
| F1 | DCBS 80 ppm | 24 | 9.5 | 8.9 | 7.9 | 7.0 | 6.3 | 5.7 | 5.2 | 4.9 | 4.7 | 4.5 | 4.1 | 3.9 | 3.9 | 3.9 | - | 9.5 | 5.9 |
| | DCBS 600 ppm | 24 | 71 | 67 | 59 | 52 | 47 | 42 | 40 | 37 | 35 | 33 | 31 | 30 | 29 | 29 | - | 71 | 44 |
| | DCBS 4500 ppm | 24 | 534 | 502 | 449 | 392 | 355 | 322 | 296 | 277 | 260 | 249 | 234 | 219 | 219 | 219 | - | 534 | 331 |

Table 10 Test substance intake of F0 and F1 parental female rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Gener- ation | Group | Number of animals | Pre-mating period | | | | | | | | | | Breeding period | | | | | | All the periods | | | |
|-----------------|---------------|-------------------------|-----------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----------------|------|-------|----------------|------|-------|-----------------|---|------|------|
| | | | Test substance intake (mg/kg/day) | | | | | | | | | | Gestation days | | | Lactation days | | | Min | - | Max | Mean |
| | | | Treatment week | | | | | | | | | | 0-7 | 7-14 | 14-20 | 0-7 | 7-14 | 14-21 | | | | |
| | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | | | | | | | | | | |
| F0 | DCBS 80 ppm | 24 | 8.3 | 7.9 | 7.2 | 6.7 | 6.3 | 6.1 | 5.9 | 5.5 | 5.3 | 5.1 | 5.3 | 5.3 | 4.3 | 8.0 | 11.5 | 16.3 | 4.3 | - | 16.3 | 7.2 |
| | DCBS 600 ppm | 24 | 62 | 59 | 53 | 51 | 48 | 46 | 44 | 42 | 41 | 39 | 42 | 41 | 33 | 59 | 86 | 121 | 33 | - | 121 | 54 |
| | DCBS 4500 ppm | 24 | 460 | 438 | 402 | 387 | 367 | 350 | 337 | 322 | 310 | 307 | 315 | 315 | 266 | 459 | 681 | 942 | 266 | - | 942 | 416 |
| F1 | DCBS 80 ppm | 24 | 9.9 | 9.3 | 8.3 | 7.6 | 7.0 | 6.6 | 6.2 | 5.9 | 5.5 | 5.5 | 5.5 | 5.5 | 4.5 | 6.7 | 10.5 | 14.3 | 4.5 | - | 14.3 | 7.4 |
| | DCBS 600 ppm | 24 | 73 | 70 | 62 | 56 | 53 | 49 | 46 | 45 | 42 | 41 | 41 | 41 | 33 | 49 | 77 | 107 | 33 | - | 107 | 55 |
| | DCBS 4500 ppm | 24 | 538 | 526 | 479 | 431 | 404 | 377 | 352 | 336 | 320 | 315 | 315 | 309 | 260 | 348 | 563 | 794 | 260 | - | 794 | 417 |

Test substance intake of females during the lactation period was expressed as the total amounts of the test substance by maternal animals and their offspring.

Table 11 Vaginal estrous cycles in F0 and F1 parental female rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Gener- ation | Group | Number of animals | Estrous cyclicity | | |
|-----------------|---------------|-------------------------|---|--------------|-----------------------|
| | | | Normality Incidence (%) ^a | Mean | Length (days) S.D. |
| F0 | Control | 24 | 24/24 (100) | Mean S.D. | 4.05 0.16 |
| | DCBS 80 ppm | 24 | 24/24 (100) | Mean S.D. | 4.01 0.06 |
| | DCBS 600 ppm | 24 | 24/24 (100) | Mean S.D. | 4.04 0.15 |
| | DCBS 4500 ppm | 24 | 24/24 (100) | Mean S.D. | 4.01 0.06 |
| F1 | Control | 24 | 23/24 (95.8) | Mean S.D. | 4.21 0.34 |
| | DCBS 80 ppm | 24 | 24/24 (100) | Mean S.D. | 4.05 0.21 |
| | DCBS 600 ppm | 24 | 23/24 (95.8) | Mean S.D. | 4.25 1.08 |
| | DCBS 4500 ppm | 24 | 24/24 (100) | Mean S.D. | 4.07 0.24 |

a: Incidence of females with the normal estrous cycle (%) = (number of females cycling normally/number of females examined) x 100.
The normal estrous cycle is defined as having a mean cycle length between 4.0 and 6.0 days.

Table 12 Reproductive findings in F0 and F1 parental rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamido (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Generation | Group | Copulation index | | Fertility index | | Gestation index | Pre-coital interval (days) | Gestation length (days) | Number of implantations | Delivery index (%) ^a | Number of pups delivered | Sex ratio | Viability index (%) ^b on postnatal day | | | |
|---------------|-------------|---------------------|-----------------------|---------------------|-----------------------|-----------------|----------------------------|-------------------------|-------------------------|---------------------------------|--------------------------|-----------|---|------|------|-------|
| | | Male (Incidence, %) | Female (Incidence, %) | Male (Incidence, %) | Female (Incidence, %) | | | | | | | | 0 | 4 | 21 | |
| F0 | Control | 24/24 | 24/24 | 22/24 | 22/24 | 22/22 | Mean | 2.4 | 22.1 | 13.5 | 94.9 | 12.8 | 0.528 | 99.0 | 98.7 | 100.0 |
| | | (100) | (100) | (91.7) | (91.7) | (100) | S.D. | 1.2 | 0.4 | 2.1 | 6.0 | 2.1 | | 2.6 | 3.6 | 0.0 |
| | DCBS 80 ppm | 23/23 | 24/24 | 23/23 | 24/24 | 24/24 | Mean | 2.8 | 22.2 | 13.9 | 94.9 | 13.2 | 0.554 | 99.3 | 98.2 | 99.0 |
| | | (100) | (100) | (100) | (100) | (100) | S.D. | 1.1 | 0.4 | 1.4 | 6.3 | 1.6 | | 2.4 | 3.1 | 3.5 |
| DCBS 600 ppm | 24/24 | 24/24 | 24/24 | 24/24 | 24/24 | Mean | 2.4 | 22.0 | 14.6 | 94.3 | 13.8 | 0.506 | 99.7 | 96.6 | 99.5 | |
| | (100) | (100) | (100) | (100) | (100) | S.D. | 1.0 | 0.3 | 1.3 | 5.4 | 1.5 | | 1.4 | 9.5 | 2.6 | |
| DCBS 4500 ppm | 24/24 | 24/24 | 24/24 | 24/24 | 24/24 | Mean | 2.4 | 22.1 | 13.2 | 94.8 | 12.5 | 0.525 | 99.0 | 97.6 | 99.5 | |
| | (100) | (100) | (100) | (100) | (100) | S.D. | 1.1 | 0.3 | 1.5 | 4.7 | 1.7 | | 2.8 | 4.7 | 2.6 | |
| | | | | | | | | | | | | | F1 pup data | | | |
| F1 | Control | 24/24 | 24/24 | 23/24 | 23/24 | 23/23 | Mean | 2.7 | 22.3 | 14.1 | 90.4 | 12.7 | 0.488 | 98.7 | 95.9 | 100.0 |
| | | (100) | (100) | (95.8) | (95.8) | (100) | S.D. | 1.0 | 0.4 | 3.2 | 13.4 | 3.6 | | 2.9 | 9.2 | 0.0 |
| | DCBS 80 ppm | 24/24 | 24/24 | 22/24 | 22/24 | 22/22 | Mean | 2.6 | 22.2 | 13.5 | 92.9 | 12.6 | 0.516 | 99.7 | 94.2 | 100.0 |
| | | (100) | (100) | (91.7) | (91.7) | (100) | S.D. | 1.4 | 0.4 | 3.7 | 5.7 | 3.7 | | 1.2 | 17.5 | 0.0 |
| DCBS 600 ppm | 22/24 | 24/24 | 20/22 | 22/24 | 21/22 | Mean | 2.6 | 22.1 | 13.0 | 88.9 | 12.0 | 0.557 | 98.3 | 93.1 | 97.0 | |
| | (91.7) | (100) | (90.9) | (91.7) | (95.5) | S.D. | 1.2 | 0.4 | 4.2 | 21.0 | 4.2 | | 4.5 | 13.0 | 8.8 | |
| DCBS 4500 ppm | 24/24 | 24/24 | 24/24 | 24/24 | 24/24 | Mean | 2.8 | 22.1 | 14.3 | 91.3 | 13.0 | 0.522 | 95.9 | 88.4 | 97.7 | |
| | (100) | (100) | (100) | (100) | (100) | S.D. | 1.7 | 0.3 | 2.1 | 11.2 | 2.4 | | 5.7 | 22.7 | 6.8 | |
| | | | | | | | | | | | | | F2 pup data | | | |
| | | | | | | | | | | | | | (22) | | | |

Copulation index (%) = (number of animals with successful copulation/number of animals paired) x 100.

Fertility index (%) = (number of animals that impregnated a female or were pregnant/number of animals with successful copulation) x 100.

Gestation index (%) = (number of females that delivered live pups/number of pregnant females) x 100.

Delivery index (%) = (number of pups delivered/number of implantations) x 100.

Sex ratio = total number of male pups/total number of pups.

Viability index on postnatal day 0 (%) = (number of live pups on postnatal day 0/number of pups delivered) x 100.

Viability index on postnatal day 4 (%) = (number of live pups on postnatal day 4/number of live pups on postnatal day 0) x 100.

Viability index on postnatal day 21 (%) = (number of live pups on postnatal day 21/number of live pups selected for use on postnatal day 4) x 100.

a and b: The litter is the unit evaluated.

Values in parentheses are the number of animals examined.

Table 13 Sperm number and motility in F0 and F1 parental male rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Gener- ation | Group | Number of animals | | Number of testis sperms | | Number of epididymal sperms | | % Motile | % Pro- gressive | Swimming speed | | | Swimming pattern | | | |
|-----------------|---------------|-------------------------|-------|----------------------------|---------------------------|--------------------------------|--------------------------|-------------|-----------------------|----------------|-------|-------|---------------------|------|------|------|
| | | | | 10 ⁶ /testis | 10 ⁶ /g testis | 10 ⁶ /cauda | 10 ⁶ /g cauda | | | VAP | VSL | VCL | ALH | BCF | STR | LIN |
| F0 | Control | 24 | Mean | 184.1 | 111.4 | 268.5 | 856.4 | 88.1 | 70.9 | 159.6 | 112.1 | 365.7 | 20.1 | 27.9 | 69.3 | 30.4 |
| | | | S.D. | 29.3 | 13.2 | 47.6 | 94.4 | 9.3 | 17.4 | 20.8 | 22.5 | 53.4 | 1.1 | 1.5 | 6.6 | 2.8 |
| | DCBS 80 ppm | 23 | Mean | 187.7 | 110.7 | 276.2 | 838.9 | 92.6 | 77.3 | 159.8 | 114.1 | 370.1 | 19.9 | 27.4 | 70.7 | 30.7 |
| | | | S.D. | 28.3 | 15.7 | 40.3 | 99.4 | 8.2 | 15.3 | 19.2 | 20.0 | 42.5 | 1.1 | 1.5 | 5.7 | 3.0 |
| DCBS 600 ppm | 24 | Mean | 184.2 | 110.6 | 269.9 | 850.3 | 93.2 | 77.4 | 162.7 | 116.1 | 372.3 | 20.0 | 27.6 | 71.0 | 31.3 | |
| | | S.D. | 32.7 | 17.1 | 56.8 | 122.1 | 5.9 | 12.1 | 22.0 | 19.3 | 49.8 | 1.3 | 2.2 | 4.3 | 2.5 | |
| DCBS 4500 ppm | 24 | Mean | 180.8 | 106.1 | 263.7 | 844.2 | 89.4 | 70.5 | 156.8 | 110.5 | 358.4 | 19.9 | 28.3 | 69.5 | 30.6 | |
| | | S.D. | 35.4 | 18.8 | 62.8 | 191.3 | 10.2 | 22.2 | 25.3 | 29.2 | 56.3 | 1.0 | 2.3 | 8.6 | 4.0 | |
| F1 | Control | 24 | Mean | 194.5 | 115.3 | 273.6 | 849.9 | 92.3 | 81.8 | 175.2 | 126.9 | 399.5 | 21.3 | 26.4 | 72.5 | 32.0 |
| | | | S.D. | 23.0 | 9.5 | 40.0 | 69.4 | 5.0 | 8.1 | 9.8 | 10.2 | 19.8 | 0.9 | 1.6 | 3.3 | 2.1 |
| | DCBS 80 ppm | 24 | Mean | 181.1 | 108.4 | 254.0 | 821.5 | 92.9 | 81.8 | 171.7 | 123.9 | 391.5 | 20.9 | 26.8 | 72.1 | 31.9 |
| | | | S.D. | 21.3 | 14.3 | 40.4 | 106.8 | 4.0 | 4.9 | 11.2 | 10.3 | 28.6 | 0.8 | 1.4 | 2.7 | 2.0 |
| | DCBS 600 ppm | 24 | Mean | 186.3 | 111.1 | 256.2 | 827.2 | 93.3 | 83.9 | 172.4 | 126.0 | 395.1 | 20.8 | 26.1 | 73.3 | 32.1 |
| | | | S.D. | 22.5 | 11.3 | 46.0 | 93.3 | 5.6 | 6.4 | 11.4 | 10.5 | 28.6 | 0.8 | 1.6 | 2.9 | 1.8 |
| | DCBS 4500 ppm | 24 | Mean | 201.0 | 113.6 | 250.3 | 807.0 | 93.0 | 82.7 | 171.3 | 125.7 | 393.6 | 20.5 * | 27.0 | 73.5 | 32.2 |
| | | | S.D. | 33.3 | 15.0 | 55.4 | 127.5 | 7.4 | 8.2 | 13.9 | 12.6 | 29.8 | 1.0 | 1.8 | 2.8 | 1.5 |

VAP: Mean path velocity (µm/sec).

VSL: Straight line average velocity (µm/sec).

VCL: Mean curvilinear velocity (µm/sec).

ALH: Mean lateral head displacement (µm).

BCF: Mean beat cross frequency (Hz).

STR: Mean straightness (%) = VSL/VAP x 100.

LIN: Mean linearity (%) = VSL/VCL x 100.

*: Significantly different from the control at p ≤ 0.05 by Dunnett's test.

Table 14. Abnormal sperm ratio in F0 and F1 parental male rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Generation | Group | Number of animals | Abnormal sperm ratio (%) | | | | | | | | | | | | | | | |
|------------|---------------|-------------------|--------------------------|----------------|-------------|---------------|---------------|------------------|-----------------------|-----------|---------|-----------|-------------|----------------|-----------|-----|-----|-----|
| | | | Total | Head | | | | | Neck and middle piece | | | Tail | | | | | | |
| | | | | Tailless sperm | Small sized | Banana shaped | Hooked shaped | Truncated shaped | Amorphous shaped | Two heads | Flexion | Two necks | Enlargement | Fragmen-tation | Two tails | | | |
| F0 | Control | 24 | Mean | 1.1 | 1.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | |
| | | | S.D. | 0.6 | 0.6 | 0.0 | 0.2 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| | DCBS 80 ppm | 23 | Mean | 1.2 | 1.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| | | | S.D. | 0.8 | 0.8 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| | DCBS 600 ppm | 24 | Mean | 2.4 | 2.2 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| | | | S.D. | 3.5 | 3.5 | 0.0 | 0.2 | 0.0 | 0.1 | 0.1 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| | DCBS 4500 ppm | 24 | Mean | 2.0 | 1.8 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| | | | S.D. | 2.4 | 2.0 | 0.0 | 0.5 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| F1 | Control | 24 | Mean | 1.4 | 1.3 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | |
| | | | S.D. | 1.3 | 1.2 | 0.0 | 0.3 | 0.0 | 0.1 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| | DCBS 80 ppm | 24 | Mean | 1.1 | 0.9 | 0.0 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | |
| | | | S.D. | 0.8 | 0.8 | 0.0 | 0.2 | 0.0 | 0.2 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| | DCBS 600 ppm | 24 | Mean | 1.2 | 1.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | |
| | | | S.D. | 1.7 | 1.6 | 0.1 | 0.2 | 0.1 | 0.1 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| | DCBS 4500 ppm | 24 | Mean | 1.6 | 1.5 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | |
| | | | S.D. | 1.9 | 1.8 | 0.1 | 0.0 | 0.0 | 0.1 | 0.1 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |

Table 15 Sexual development in F1 parental rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Gener- ation | Group | Male | | | | Female | | | |
|-----------------|---------------|-------------------------|------|---------------------------------------|--|-------------------------|------|----------------------------------|---|
| | | Number of animals | | Age at preputial separation (days) | Body weight (g) on the day at preputial separation | Number of animals | | Age at vaginal opening (days) | Body weight (g) on the day at vaginal opening |
| F1 | Control | 24 | Mean | 41.3 | 226.9 | 24 | Mean | 29.6 | 104.6 |
| | | | S.D. | 1.6 | 20.3 | | S.D. | 1.0 | 9.4 |
| | DCBS 80 ppm | 24 | Mean | 41.4 | 226.5 | 24 | Mean | 30.0 | 109.1 |
| | | | S.D. | 1.6 | 18.5 | | S.D. | 1.7 | 10.6 |
| | DCBS 600 ppm | 24 | Mean | 41.8 | 228.3 | 24 | Mean | 31.2 ^{SS} | 112.1 * |
| | | | S.D. | 1.6 | 17.0 | | S.D. | 1.7 | 13.8 |
| | DCBS 4500 ppm | 24 | Mean | 42.8 ** | 229.6 | 24 | Mean | 31.1 ^{SS} | 112.3 * |
| | | | S.D. | 1.5 | 17.5 | | S.D. | 1.3 | 9.1 |

*: Significantly different from the control at $p \leq 0.05$ by Dunnett's test.

**: Significantly different from the control at $p \leq 0.01$ by Dunnett's test.

^{SS}: Significantly different from the control at $p \leq 0.01$ by Mann-Whitney U-test.

Table 16 Locomotor activity count in F1 parental male rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Generation | Group | Number of animals | Locomotor activity count | | | | | | | |
|------------|---------------|-------------------|------------------------------|-------|-------|-------|-------|-------|------|-------|
| | | | Determination time (minutes) | | | | | | | |
| | | | 0-10 | 10-20 | 20-30 | 30-40 | 40-50 | 50-60 | 0-60 | |
| F1 | Control | 10 | Mean | 206.0 | 76.8 | 26.3 | 14.3 | 5.3 | 0.8 | 329.5 |
| | | | S.D. | 58.9 | 40.7 | 25.0 | 30.6 | 16.8 | 2.2 | 126.7 |
| | DCBS 80 ppm | 10 | Mean | 248.8 | 63.1 | 34.2 | 9.6 | 11.0 | 1.6 | 368.3 |
| | | | S.D. | 78.8 | 35.7 | 32.6 | 14.3 | 19.7 | 5.1 | 146.2 |
| | DCBS 600 ppm | 10 | Mean | 208.7 | 78.9 | 58.1 | 52.2 | 12.0 | 14.7 | 424.6 |
| | | | S.D. | 111.6 | 63.7 | 71.3 | 89.1 | 28.2 | 31.6 | 230.1 |
| | DCBS 4500 ppm | 10 | Mean | 204.6 | 72.2 | 20.9 | 11.5 | 1.0 | 0.0 | 310.2 |
| | | | S.D. | 154.5 | 86.4 | 20.1 | 17.0 | 2.5 | 0.0 | 236.3 |

Table 17 Locomotor activity count in F1 parental female rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Gener- ation | Group | Number of animals | Locomotor activity count | | | | | | | |
|-----------------|---------------|-------------------------|------------------------------|-------|-------|-------|-------|-------|------|-------|
| | | | Determination time (minutes) | | | | | | | |
| | | | 0-10 | 10-20 | 20-30 | 30-40 | 40-50 | 50-60 | 0-60 | |
| F1 | Control | 10 | Mean | 168.3 | 55.7 | 23.6 | 10.1 | 1.8 | 0.5 | 260.0 |
| | | | S.D. | 66.1 | 42.3 | 27.4 | 20.6 | 5.7 | 1.6 | 115.6 |
| | DCBS 80 ppm | 10 | Mean | 212.0 | 59.3 | 34.8 | 19.7 | 11.2 | 0.0 | 337.0 |
| | | | S.D. | 121.3 | 46.5 | 75.6 | 54.4 | 35.4 | 0.0 | 297.9 |
| | DCBS 600 ppm | 10 | Mean | 220.2 | 74.3 | 25.7 | 9.1 | 4.5 | 0.8 | 334.6 |
| | | | S.D. | 103.7 | 48.9 | 32.7 | 26.1 | 11.7 | 2.5 | 181.6 |
| | DCBS 4500 ppm | 10 | Mean | 203.1 | 52.6 | 19.7 | 14.5 | 6.6 | 0.0 | 296.5 |
| | | | S.D. | 109.8 | 42.2 | 21.8 | 34.9 | 20.9 | 0.0 | 173.4 |

Table 18 Data on learning tests in F1 parental male rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Gener- ation | Group | Number of animals | | Time for maze trials (sec) | | | | Number of errors for maze trials | | | |
|-----------------|---------------|-------------------------|------|----------------------------|-------|-------|-------|----------------------------------|-------|-------|-------|
| | | | | Day 1 | Day 2 | Day 3 | Day 4 | Day 1 | Day 2 | Day 3 | Day 4 |
| F1 | Control | 10 | Mean | 8.2 | 58.0 | 29.0 | 30.9 | 0.0 | 10.2 | 2.8 | 2.8 |
| | | | S.D. | 2.4 | 35.1 | 9.8 | 12.1 | 0.1 | 7.2 | 1.8 | 2.0 |
| | DCBS 80 ppm | 10 | Mean | 8.1 | 47.1 | 23.6 | 19.8 | 0.1 | 8.5 | 3.0 | 1.3 |
| | | | S.D. | 1.2 | 20.5 | 7.0 | 7.9 | 0.1 | 2.2 | 1.7 | 0.9 |
| | DCBS 600 ppm | 10 | Mean | 8.9 | 46.3 | 35.1 | 26.7 | 0.1 | 7.8 | 5.1 | 2.6 |
| | | | S.D. | 1.9 | 19.6 | 16.1 | 11.8 | 0.1 | 2.9 | 3.9 | 2.2 |
| | DCBS 4500 ppm | 10 | Mean | 8.7 | 58.2 | 30.7 | 27.0 | 0.0 | 10.8 | 4.3 | 2.4 |
| | | | S.D. | 2.1 | 23.1 | 11.5 | 7.6 | 0.1 | 4.1 | 2.5 | 1.7 |

Day 1 : Used a straight channel.
Days 2-4 : Used a multiple T-maze.

Table 19 Data on learning tests in F1 parental female rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Gener- ation | Group | Number of animals | | Time for maze trials (sec) | | | | Number of errors for maze trials | | | |
|-----------------|---------------|-------------------------|------|----------------------------|--------|-------|-------|----------------------------------|-------|-------|-------|
| | | | | Day 1 | Day 2 | Day 3 | Day 4 | Day 1 | Day 2 | Day 3 | Day 4 |
| F1 | Control | 10 | Mean | 10.9 | 36.8 | 31.8 | 19.8 | 0.2 | 6.1 | 4.5 | 2.9 |
| | | | S.D. | 3.4 | 12.4 | 21.7 | 5.8 | 0.2 | 2.6 | 3.3 | 1.4 |
| | DCBS 80 ppm | 10 | Mean | 8.8 | 41.9 | 27.6 | 25.2 | 0.1 | 6.8 | 3.9 | 3.6 |
| | | | S.D. | 2.6 | 15.1 | 12.9 | 13.1 | 0.2 | 2.5 | 2.5 | 4.3 |
| | DCBS 600 ppm | 10 | Mean | 9.7 | 57.7 * | 36.6 | 28.1 | 0.2 | 8.3 | 5.3 | 3.7 |
| | | | S.D. | 4.0 | 18.7 | 17.9 | 14.2 | 0.4 | 2.7 | 2.9 | 3.4 |
| | DCBS 4500 ppm | 10 | Mean | 10.2 | 57.7 * | 39.5 | 31.5 | 0.2 | 9.4 * | 5.6 | 3.2 |
| | | | S.D. | 2.5 | 17.8 | 17.7 | 18.7 | 0.2 | 2.8 | 3.4 | 2.8 |

Day 1 : Used a straight channel.

Days 2-4 : Used a multiple T-maze.

*: Significantly different from the control at $p \leq 0.05$ by Dunnett's test.

Table 20 Hematological findings in F0 and F1 parental male rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Gener- ation | Group | Number of animals | WBC 10 ² /μL | Differential count of WBC % | | | | | | | | |
|-----------------|---------------|-------------------------|----------------------------|-----------------------------|----------------|-----------------|---------------|---------------|-----------------|--------|------|------|
| | | | | Neutrophil | | Eosino- phil | Baso- phil | Mono- cyte | Lympho- cyte | Others | | |
| | | | | Stab form | Seg- mented | | | | | | | |
| F0 | Control | 10 | Mean | 92 | 0.96 | 12.64 | 1.16 | 0.00 | 2.72 | 82.5 | 0.00 | |
| | | | S.D. | 22 | 0.63 | 5.11 | 0.64 | 0.00 | 1.08 | 5.2 | 0.00 | |
| | DCBS 80 ppm | 10 | Mean | 83 | 0.92 | 8.88 | 1.12 | 0.00 | 2.52 | 86.6 | 0.00 | |
| | | | S.D. | 17 | 0.33 | 2.38 | 0.75 | 0.00 | 0.84 | 2.4 | 0.00 | |
| | DCBS 600 ppm | 10 | Mean | 96 | 0.88 | 9.28 | 1.84 | 0.00 | 2.48 | 85.5 | 0.00 | |
| | | | S.D. | 26 | 0.41 | 3.62 | 0.97 | 0.00 | 0.92 | 3.5 | 0.00 | |
| | DCBS 4500 ppm | 10 | Mean | 111 | 0.52 | 9.12 | 1.44 | 0.00 | 2.00 | 86.9 * | 0.00 | |
| | | | S.D. | 32 | 0.53 | 3.28 | 0.85 | 0.00 | 0.68 | 3.9 | 0.00 | |
| | F1 | Control | 10 | Mean | 104 | 0.76 | 11.16 | 1.24 | 0.00 | 2.64 | 84.2 | 0.00 |
| | | | | S.D. | 17 | 0.40 | 3.45 | 0.87 | 0.00 | 0.95 | 4.5 | 0.00 |
| | | DCBS 80 ppm | 10 | Mean | 103 | 0.68 | 9.96 | 1.12 | 0.00 | 3.28 | 85.0 | 0.00 |
| | | | | S.D. | 13 | 0.50 | 3.71 | 0.73 | 0.00 | 1.46 | 4.9 | 0.00 |
| DCBS 600 ppm | | 10 | Mean | 126 | 0.84 | 9.32 | 0.92 | 0.08 | 2.44 | 86.4 | 0.00 | |
| | | | S.D. | 33 | 0.48 | 4.68 | 0.60 | 0.17 | 1.43 | 6.1 | 0.00 | |
| DCBS 4500 ppm | | 10 | Mean | 109 | 0.48 | 8.96 | 0.76 | 0.04 | 2.64 | 87.1 | 0.00 | |
| | | | S.D. | 25 | 0.37 | 3.91 | 0.61 | 0.13 | 0.87 | 3.5 | 0.00 | |

*: Significantly different from the control at $p \leq 0.05$ by Dunnett's test.

Table 21 Hematological findings in F0 and F1 parental female rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Gener- ation | Group | Number of animals | WBC 10 ² /μL | Differential count of WBC % | | | | | | | |
|-----------------|---------------|-------------------------|----------------------------|-----------------------------|----------------|-----------------|---------------|---------------|-----------------|--------|------|
| | | | | Neutrophil | | Eosino- phil | Baso- phil | Mono- cyte | Lympho- cyte | Others | |
| | | | | Stab form | Seg- mented | | | | | | |
| F0 | Control | 10 | Mean | 87 | 1.56 | 20.68 | 2.20 | 0.04 | 4.44 | 71.1 | 0.00 |
| | | | S.D. | 19 | 0.91 | 6.78 | 1.44 | 0.13 | 1.42 | 7.8 | 0.00 |
| | DCBS 80 ppm | 10 | Mean | 74 | 1.72 | 21.40 | 1.44 | 0.00 | 3.48 | 72.0 | 0.00 |
| | | | S.D. | 17 | 0.92 | 5.71 | 0.95 | 0.00 | 1.46 | 6.2 | 0.00 |
| | DCBS 600 ppm | 10 | Mean | 98 | 1.24 | 22.08 | 1.24 | 0.00 | 3.44 | 72.0 | 0.00 |
| | | | S.D. | 21 | 0.74 | 8.59 | 0.61 | 0.00 | 2.16 | 10.1 | 0.00 |
| | DCBS 4500 ppm | 10 | Mean | 76 | 1.68 | 21.92 | 1.60 | 0.00 | 3.52 | 71.3 | 0.00 |
| | | | S.D. | 17 | 0.96 | 10.81 | 0.82 | 0.00 | 1.63 | 11.8 | 0.00 |
| F1 | Control | 10 | Mean | 98 | 1.48 | 19.52 | 1.00 | 0.04 | 3.40 | 74.6 | 0.00 |
| | | | S.D. | 20 | 0.50 | 5.76 | 0.43 | 0.13 | 2.02 | 5.9 | 0.00 |
| | DCBS 80 ppm | 10 | Mean | 90 | 1.12 | 19.72 | 0.72 | 0.00 | 2.60 | 75.8 | 0.00 |
| | | | S.D. | 17 | 0.65 | 8.13 | 0.59 | 0.00 | 1.10 | 8.2 | 0.00 |
| | DCBS 600 ppm | 10 | Mean | 96 | 1.28 | 13.48 | 0.48 | 0.04 | 1.88 | 82.8 * | 0.00 |
| | | | S.D. | 26 | 0.73 | 6.32 | 0.56 | 0.13 | 1.07 | 6.7 | 0.00 |
| | DCBS 4500 ppm | 10 | Mean | 98 | 1.24 | 17.40 | 0.84 | 0.00 | 3.04 | 77.5 | 0.00 |
| | | | S.D. | 24 | 0.58 | 4.58 | 0.61 | 0.00 | 2.18 | 6.0 | 0.00 |

*: Significantly different from the control at $p \leq 0.05$ by Dunnett's test.

Table 22 Blood chemical findings in F0 and F1 parental male rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Generation | Group | Number of animals | | TP g/dL | Albumin g/dL | Globulin g/dL | |
|---------------|---------------|-------------------|------|------------|-----------------|------------------|------|
| F0 | Control | 10 | Mean | 6.27 | 2.43 | 3.84 | |
| | | | S.D. | 0.32 | 0.13 | 0.31 | |
| | DCBS 80 ppm | 10 | Mean | 6.31 | 2.43 | 3.88 | |
| | | | S.D. | 0.21 | 0.09 | 0.18 | |
| | DCBS 600 ppm | 10 | Mean | 6.33 | 2.40 | 3.93 | |
| | | | S.D. | 0.31 | 0.12 | 0.28 | |
| | DCBS 4500 ppm | 10 | Mean | 6.54 | 2.49 | 4.05 | |
| | | | S.D. | 0.28 | 0.07 | 0.24 | |
| | F1 | Control | 10 | Mean | 6.07 | 2.29 | 3.78 |
| | | | | S.D. | 0.26 | 0.12 | 0.24 |
| | | DCBS 80 ppm | 10 | Mean | 6.15 | 2.31 | 3.84 |
| | | | | S.D. | 0.31 | 0.11 | 0.25 |
| DCBS 600 ppm | | 10 | Mean | 6.26 | 2.31 | 3.95 | |
| | | | S.D. | 0.23 | 0.13 | 0.29 | |
| DCBS 4500 ppm | | 10 | Mean | 6.16 | 2.31 | 3.85 | |
| | | | S.D. | 0.26 | 0.07 | 0.27 | |

Table 23 Blood chemical findings in F0 and F1 parental female rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

| Generation | Group | Number of animals | | TP g/dL | Albumin g/dL | Globulin g/dL |
|------------|---------------|-------------------|------|------------|-----------------|------------------|
| F0 | Control | 10 | Mean | 6.45 | 2.71 | 3.74 |
| | | | S.D. | 0.27 | 0.14 | 0.25 |
| | DCBS 80 ppm | 10 | Mean | 6.80 | 2.78 | 4.02 |
| | | | S.D. | 0.43 | 0.19 | 0.29 |
| | DCBS 600 ppm | 10 | Mean | 6.28 | 2.60 | 3.68 |
| | | | S.D. | 0.30 | 0.17 | 0.22 |
| | DCBS 4500 ppm | 10 | Mean | 6.45 | 2.65 | 3.80 |
| | | | S.D. | 0.39 | 0.16 | 0.25 |
| F1 | Control | 10 | Mean | 6.36 | 2.66 | 3.70 |
| | | | S.D. | 0.33 | 0.13 | 0.25 |
| | DCBS 80 ppm | 10 | Mean | 6.34 | 2.61 | 3.73 |
| | | | S.D. | 0.41 | 0.14 | 0.27 |
| | DCBS 600 ppm | 10 | Mean | 6.23 | 2.59 | 3.64 |
| | | | S.D. | 0.37 | 0.20 | 0.25 |
| | DCBS 4500 ppm | 10 | Mean | 6.39 | 2.63 | 3.76 |
| | | | S.D. | 0.33 | 0.15 | 0.23 |