

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

*: Significantly different from the control at $p \leq 0.05$.
 **: Significantly different from the control at $p \leq 0.01$.

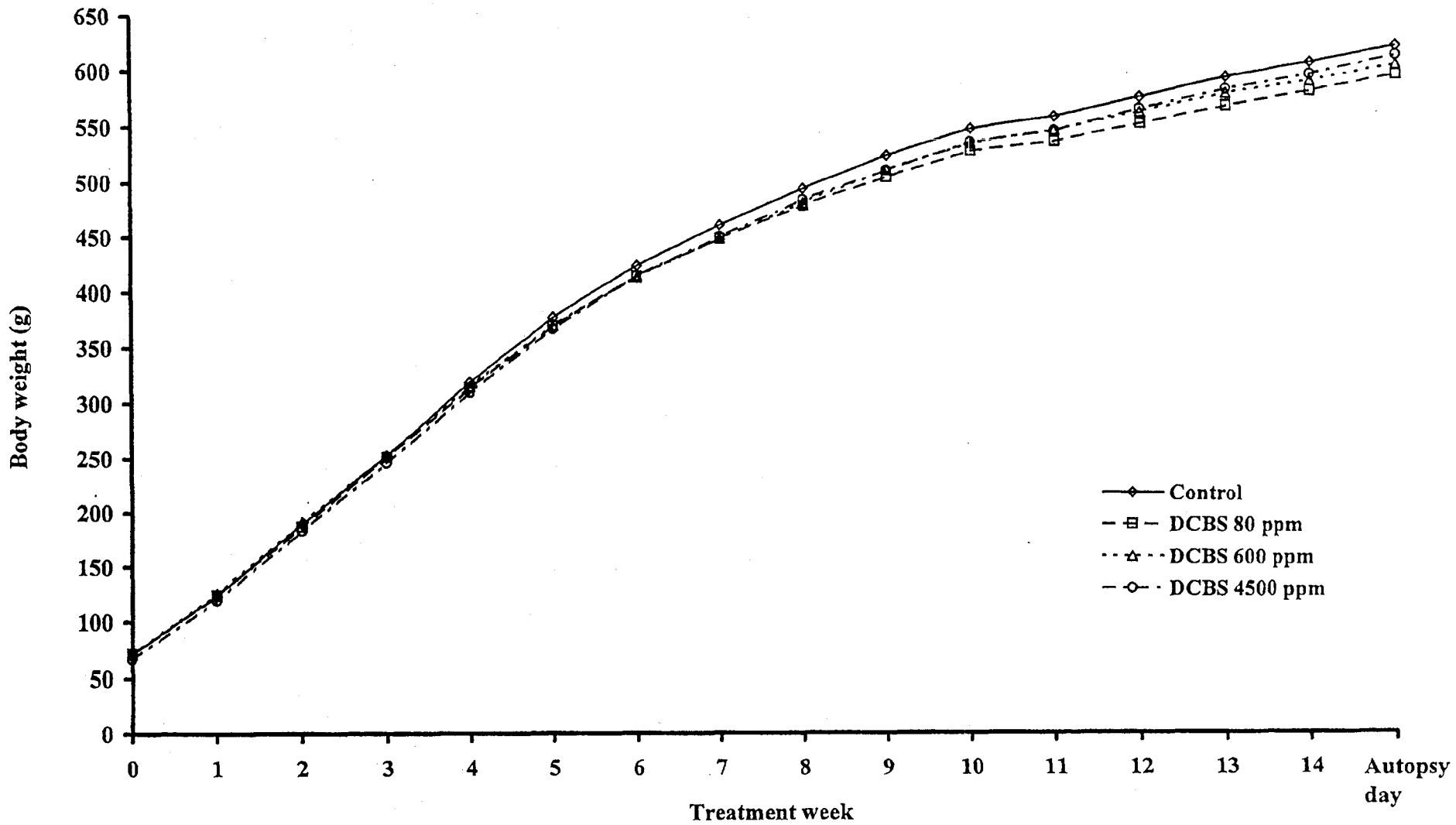


Figure 3 Body weights of F1 parental male rats in the two-generation reproductive toxicity study with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) (SR05241)

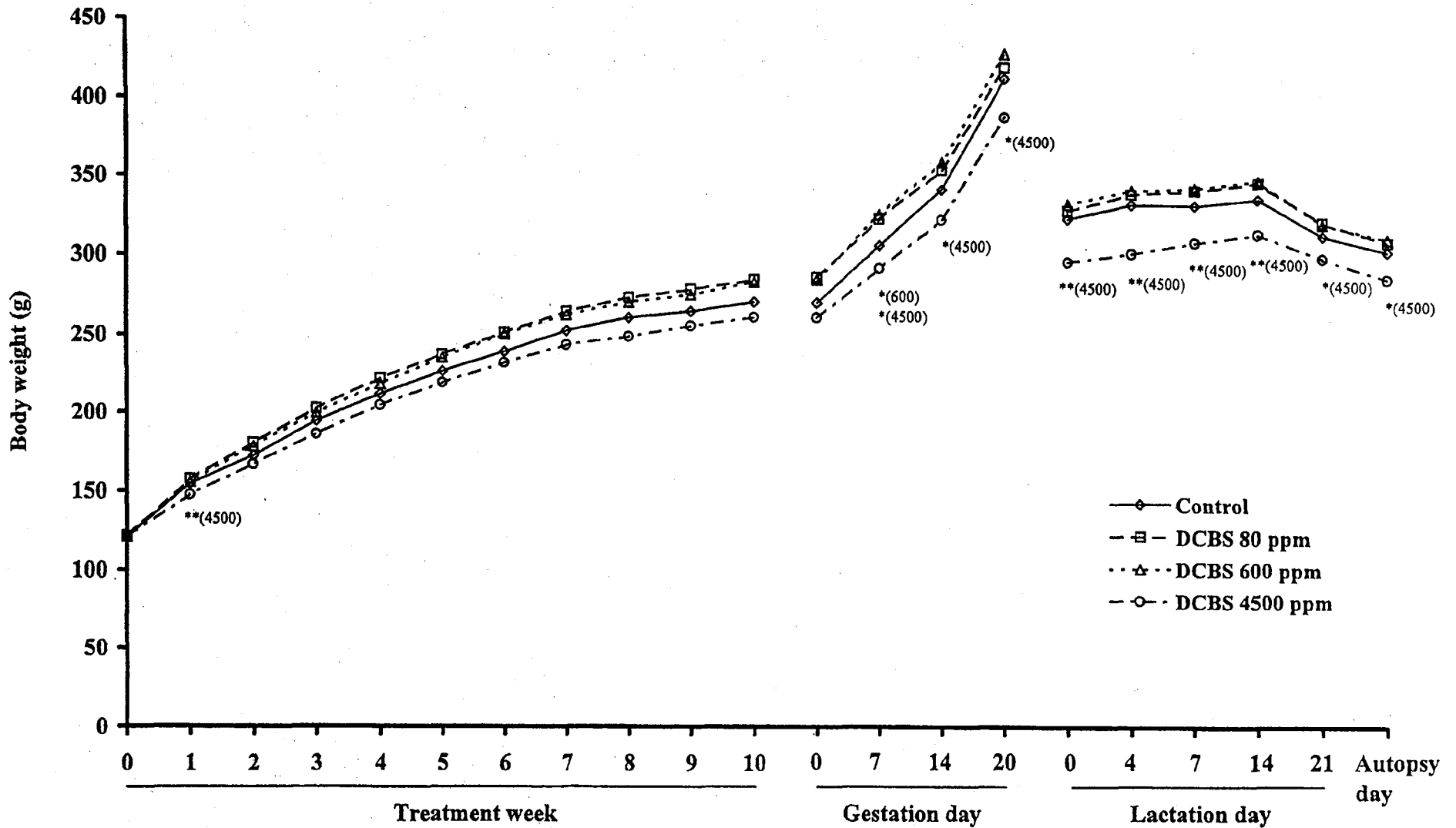


Figure 4. Body weights of F0 parental female rats in the two-generation reproductive toxicity study with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) (SR05241)

*: Significantly different from the control at $p \leq 0.05$.

**: Significantly different from the control at $p \leq 0.01$.

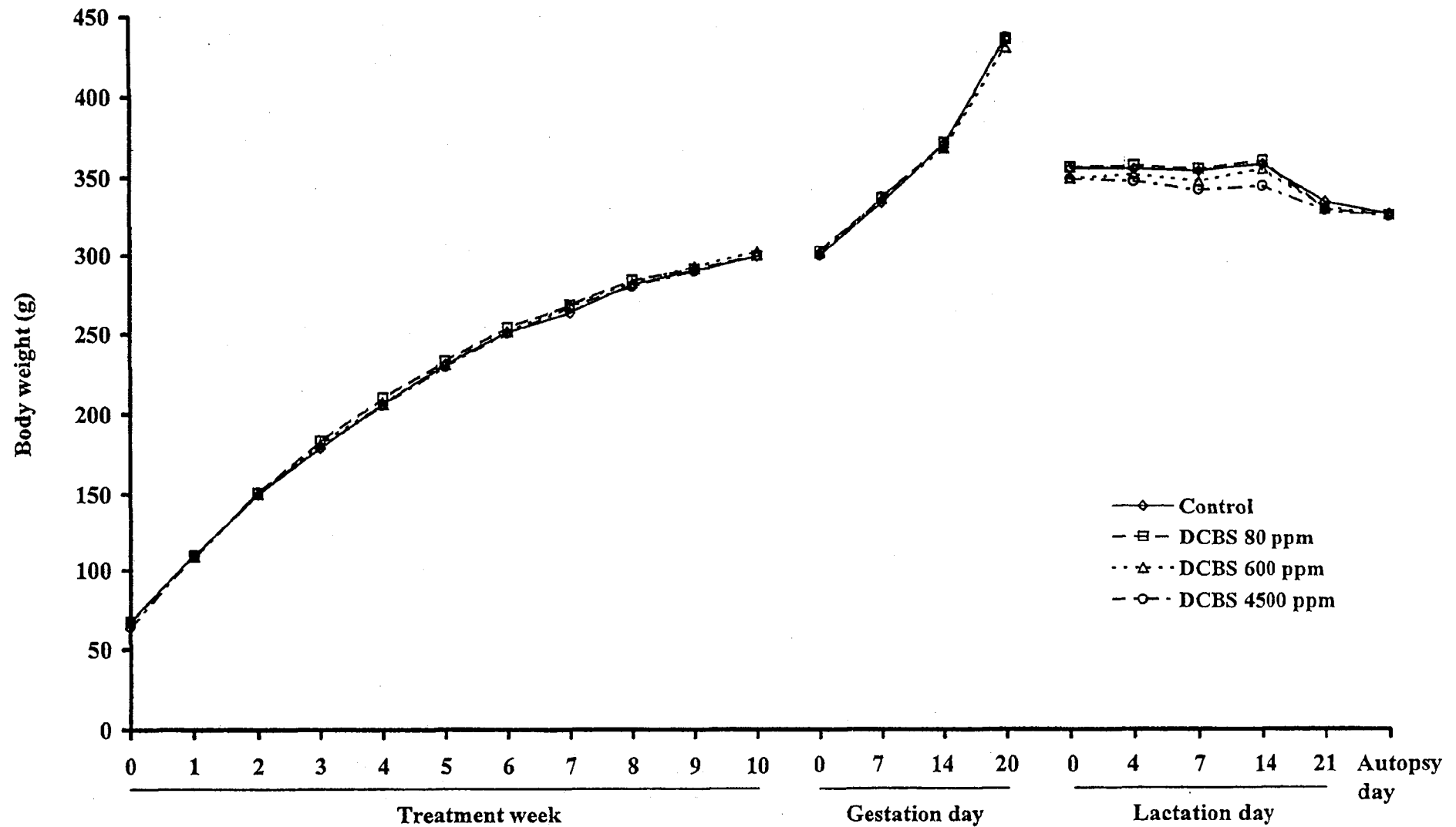


Figure 5 Body weights of F1 parental female rats in the two-generation reproductive toxicity study with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) (SR05241)

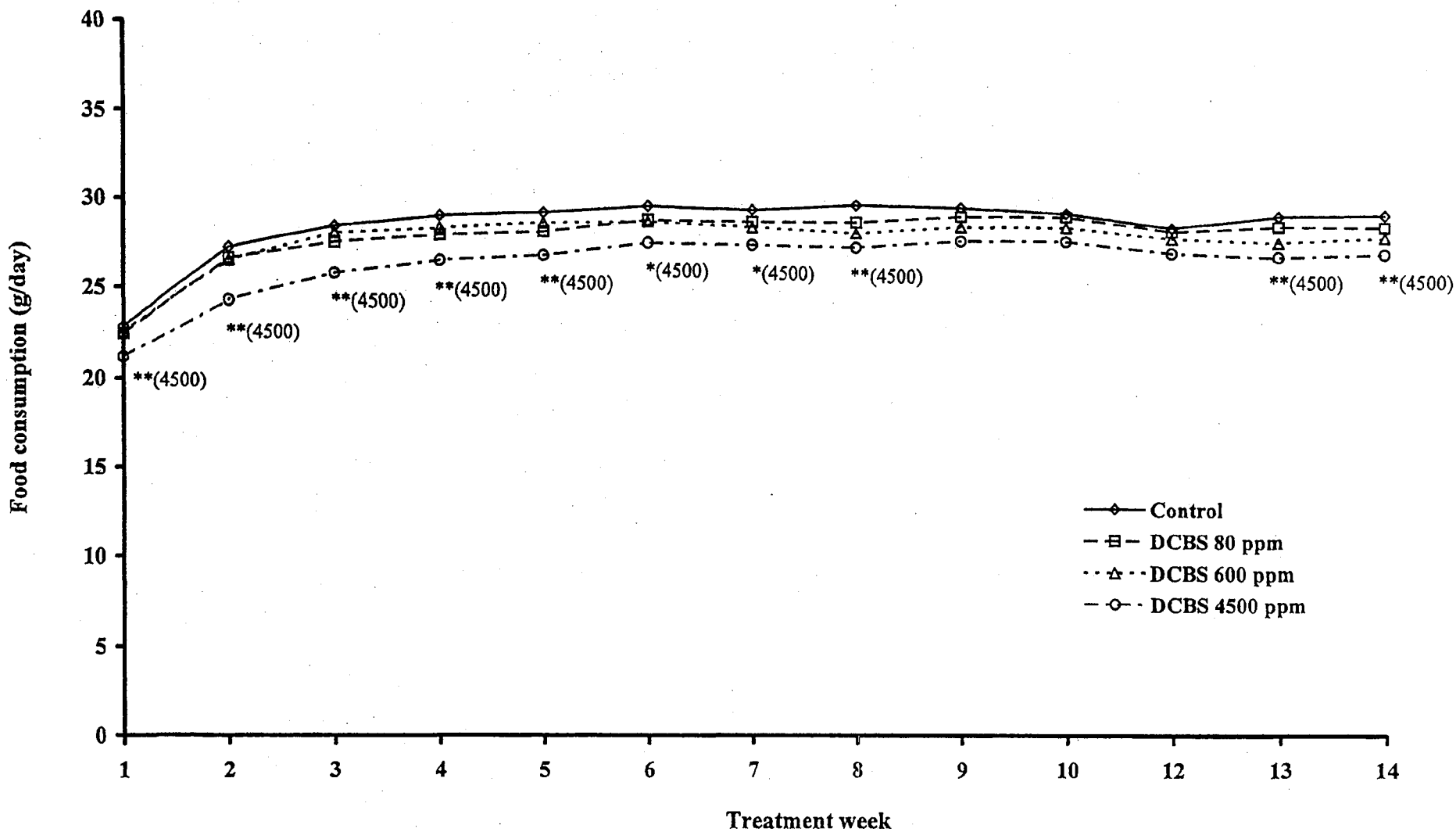


Figure 6 Food consumption of F0 parental male rats in the two-generation reproductive toxicity study with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) (SR05241)

*: Significantly different from the control at $p \leq 0.05$.

** : Significantly different from the control at $p \leq 0.01$.

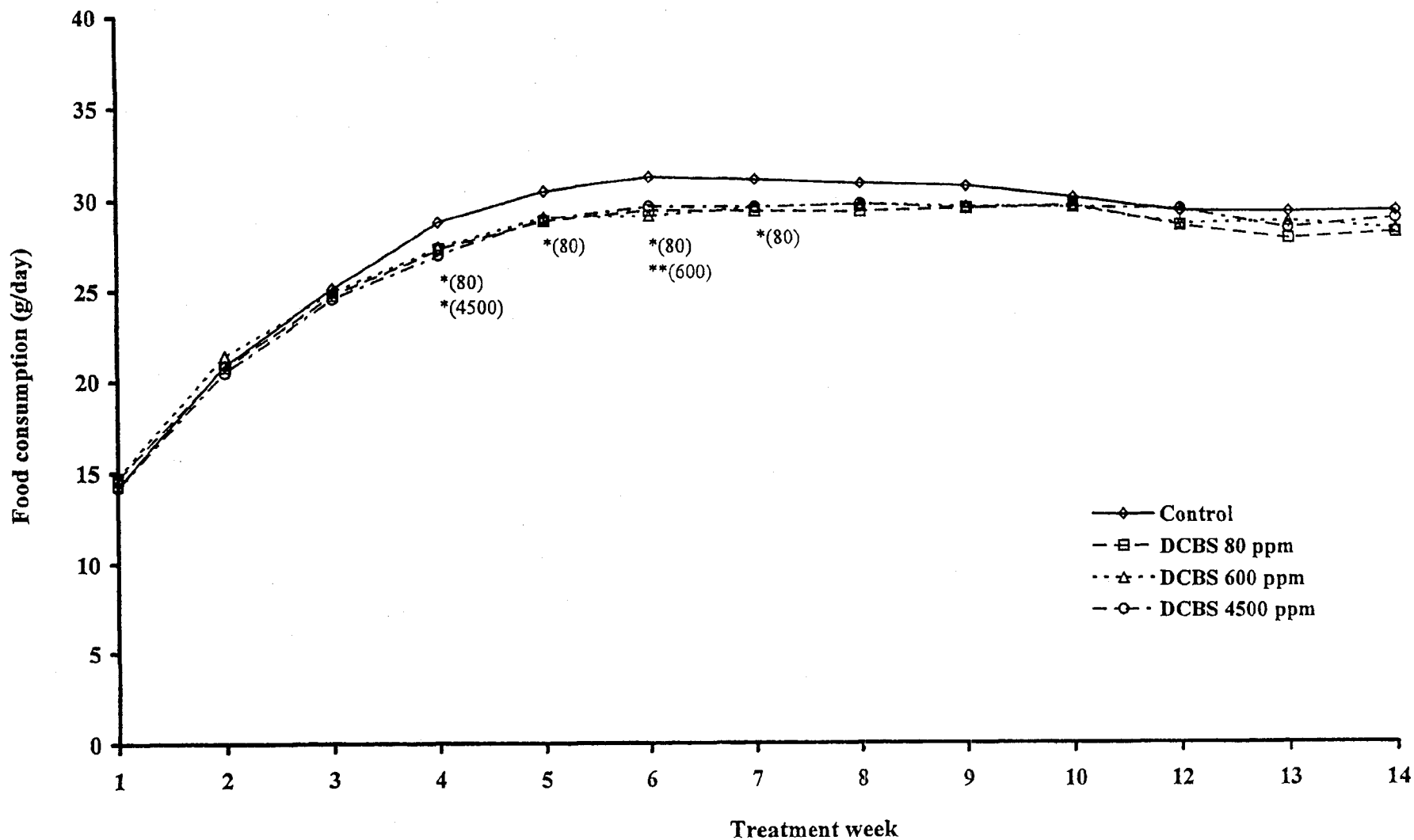


Figure 7 Food consumption of F1 parental male rats in the two-generation reproductive toxicity study with N,N-Dicyclohexyl-2-benzothiazolesulfenamido (DCBS) (SR05241)

*: Significantly different from the control at $p \leq 0.05$.
**: Significantly different from the control at $p \leq 0.01$.

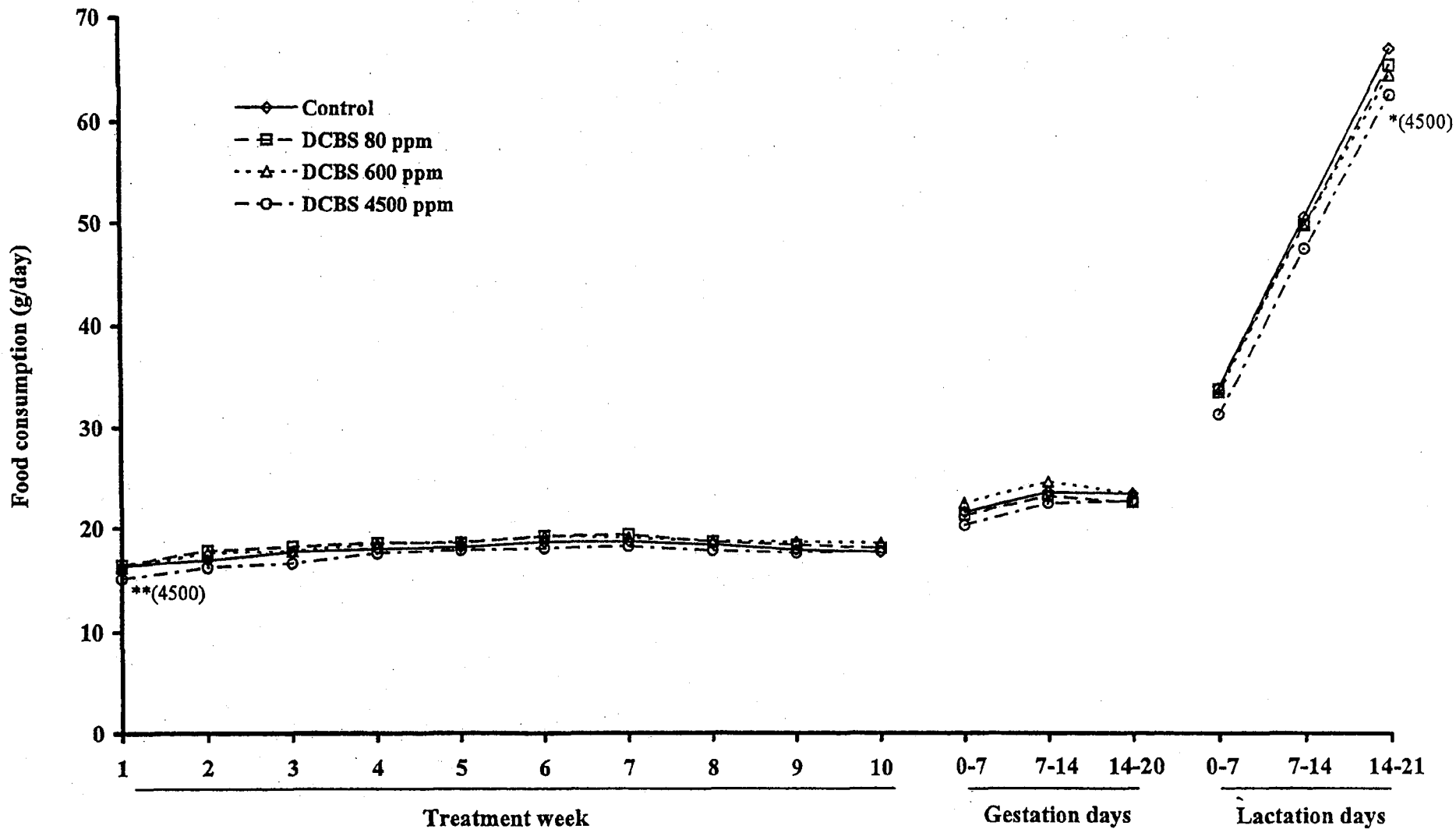


Figure 8 Food consumption of F0 parental female rats in the two-generation reproductive toxicity study with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) (SR05241)

*: Significantly different from the control at $p \leq 0.05$.

** : Significantly different from the control at $p \leq 0.01$.

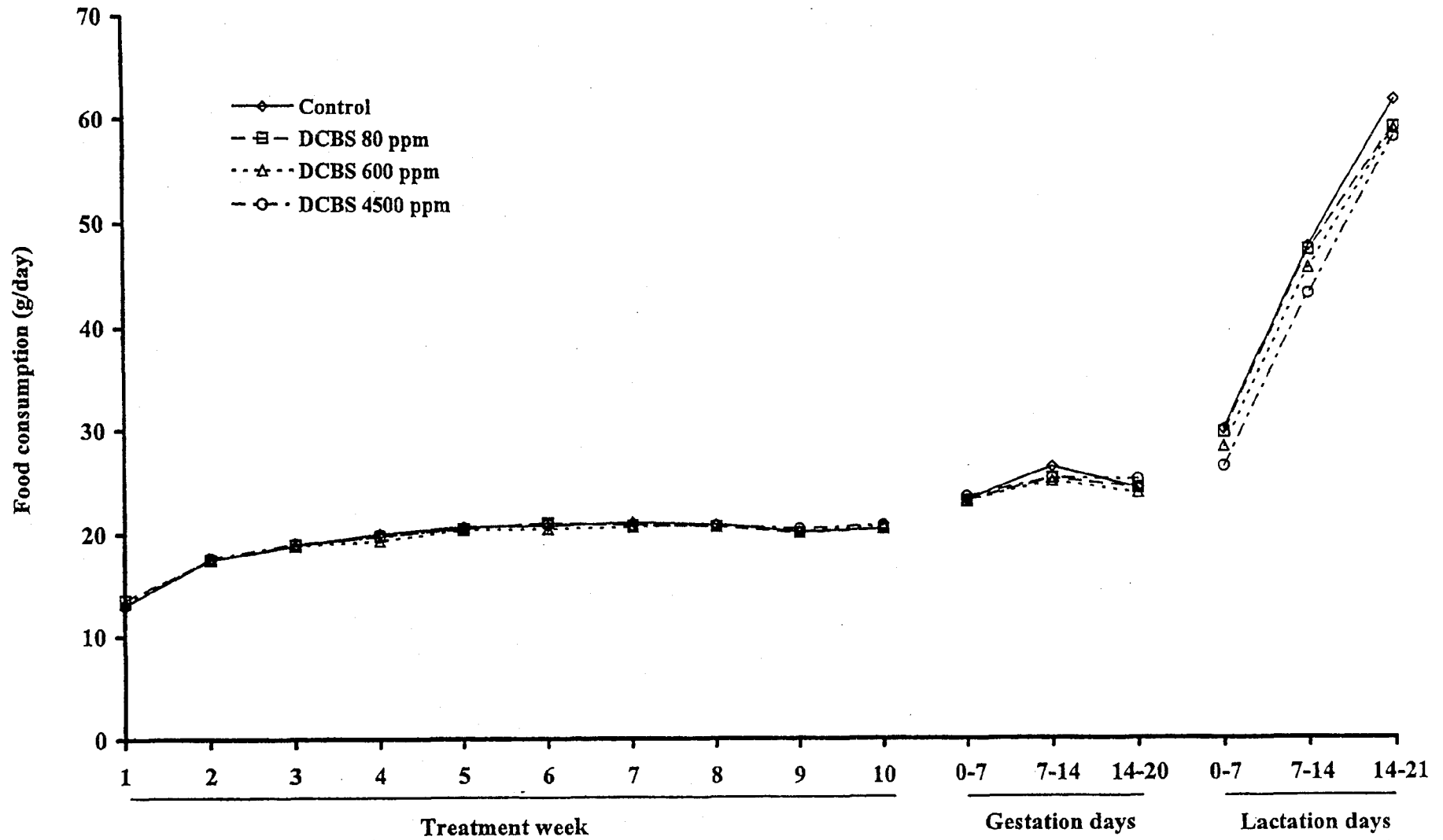


Figure 9 Food consumption of F1 parental female rats in the two-generation reproductive toxicity study with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) (SR05241)

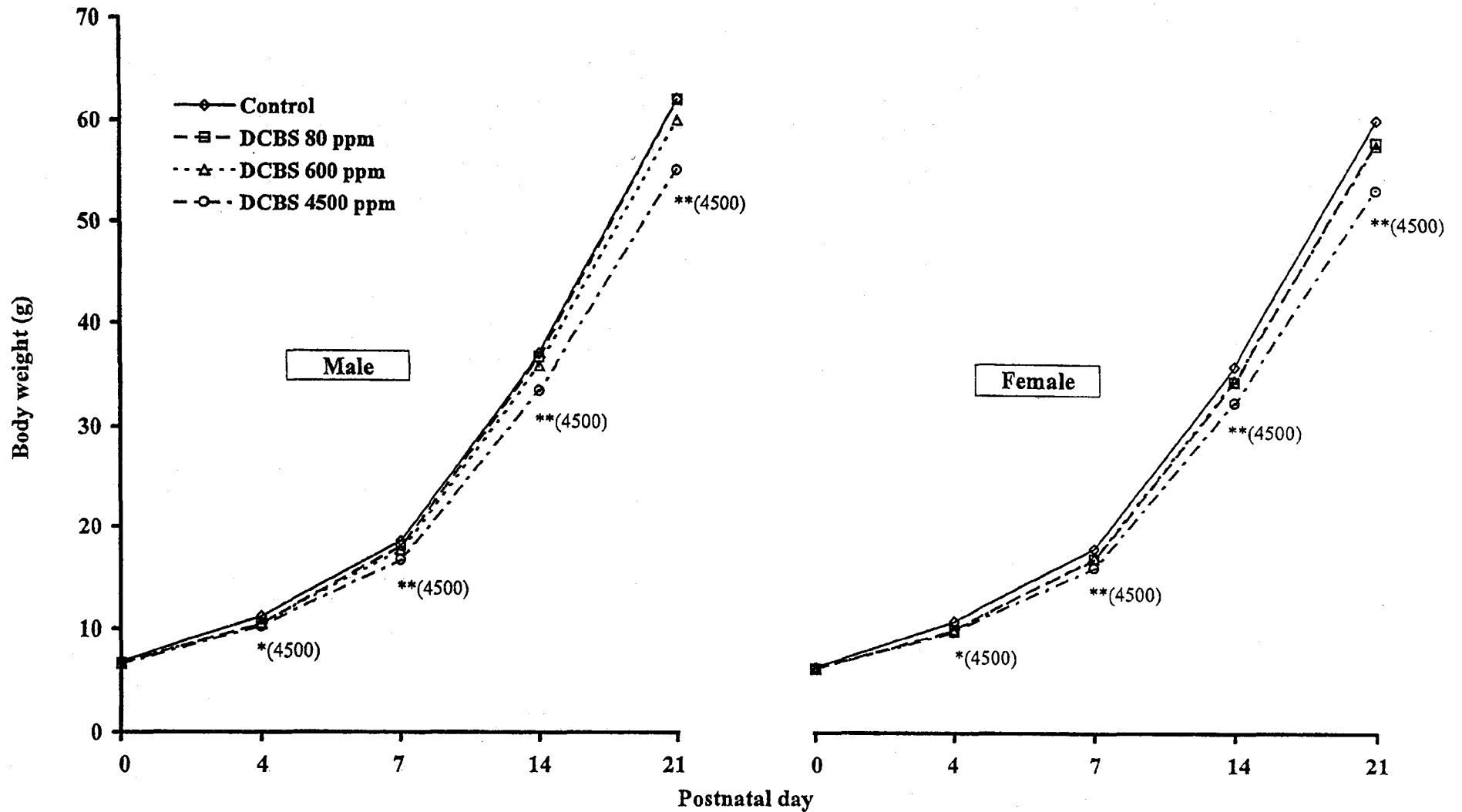


Figure 10 Body weights of F1 rat pups in the two-generation reproductive toxicity study with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) (SR05241)

*: Significantly different from the control at $p \leq 0.05$.
**: Significantly different from the control at $p \leq 0.01$.

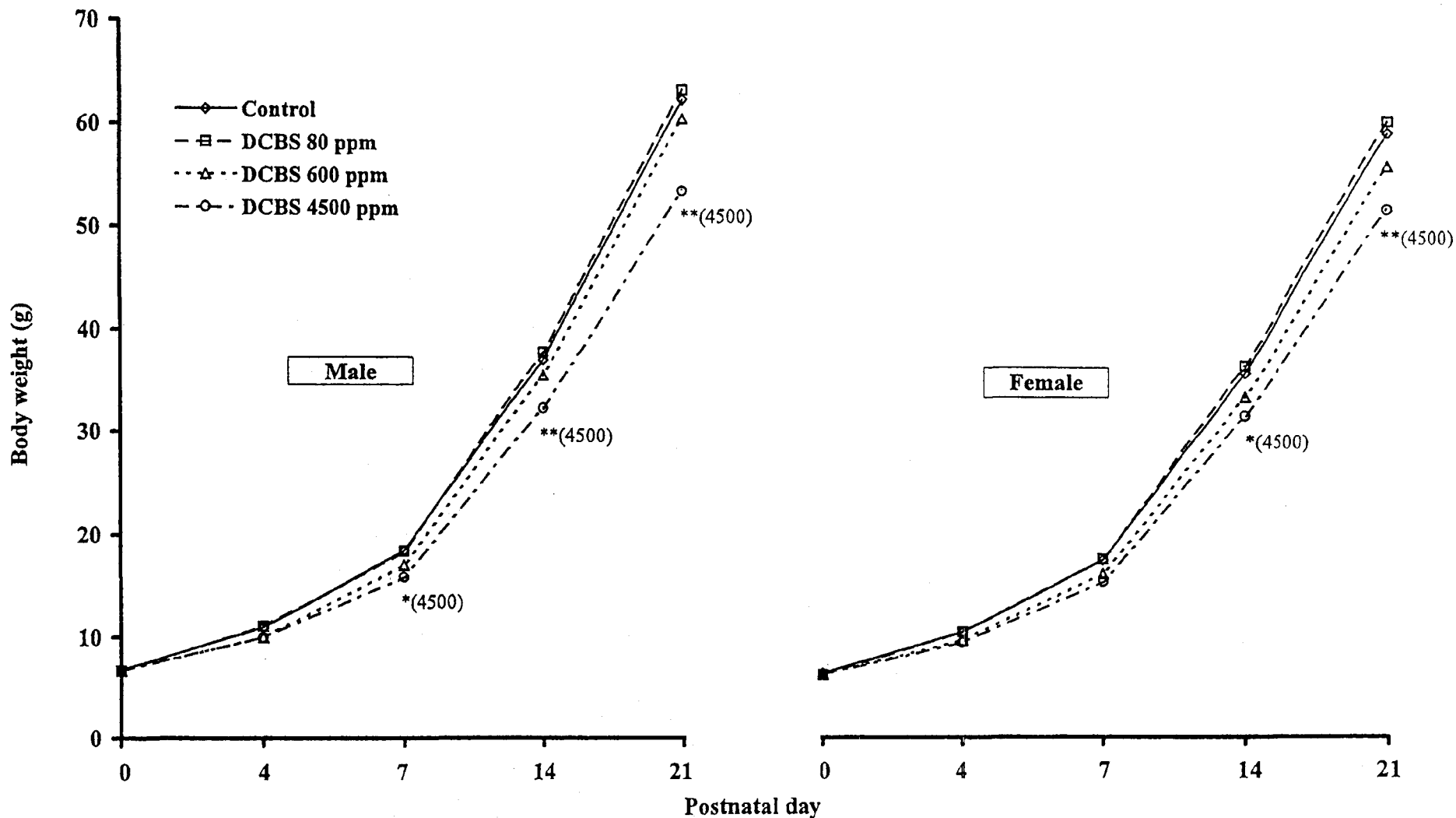


Figure 11 Body weights of F2 rat pups in the two-generation reproductive toxicity study with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) (SR05241)

*: Significantly different from the control at $p \leq 0.05$.

** : Significantly different from the control at $p \leq 0.01$.

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

Tables (1/3)

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

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

Tables (2/3)

- 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)
- 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)
- 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)
- 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)
- 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)
- 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)
- 24 Serum hormone levels in F0 and F1 parental male rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)
- 25 Serum hormone levels in F0 and F1 parental female rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)
- 26 Autopsy findings in F0 and F1 parental male rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)
- 27 Autopsy findings in F0 and F1 parental female rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)
- 28 Absolute and relative organ weights in F0 and F1 parental male rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)
- 29 Absolute and relative organ weights in F0 and F1 parental female rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)
- 30 Histopathological findings in F0 and F1 parental male rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)
- 31 Histopathological findings in F0 and F1 parental female rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)
- 32 Number of primordial follicles in F1 parental female rats treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

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

Tables (3/3)

- 33 General appearance in F1 and F2 male rat pups and weanlings during postnatal days 0-26 treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)
- 34 General appearance in F1 and F2 female rat pups and weanlings during postnatal days 0-26 treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)
- 35 Body weights of F1 and F2 rat pups treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)
- 36 Anogenital distance of F1 and F2 rat pups on postnatal day 4 treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)
- 37 Physical development in F1 and F2 rat pups treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)
- 38 Reflex response tests in F1 and F2 rat pups treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)
- 39 Autopsy findings in F1 and F2 male rat pups euthanized on postnatal day 4 or found dead on postnatal days 0-4 treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)
- 40 Autopsy findings in F1 and F2 female rat pups euthanized on postnatal day 4 or found dead on postnatal days 0-4 treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)
- 41 Autopsy findings in F1 and F2 male rat weanlings euthanized on postnatal day 26 or animals found dead on postnatal days 5-26 treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)
- 42 Autopsy findings in F1 and F2 female rat weanlings euthanized on postnatal day 26 or animals found dead on postnatal days 5-26 treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)
- 43 Absolute and relative organ weights in F1 and F2 male rat weanlings treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)
- 44 Absolute and relative organ weights in F1 and F2 female rat weanlings treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)
- 45 Histopathological findings in F1 and F2 rat weanlings treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

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.

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)

Generation	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	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 periocular 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 periocular 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						
															(23)	(23)	(23)	(23)	(23)						
		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 **	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							Autopsy day			
			Treatment week											Gestation day				Lactation 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	28.8	33.4	33.6	37.2	34.0	31.0	34.0	33.5	32.0	28.5
	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										0-11	0-12	0-13	0-14	
				0-1	0-2	0-3	0-4	0-5	0-6	0-7	0-8	0-9	0-10					
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	394.0	411.0	428.0	442.4	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-benzothiazolesulfenamamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

Generation	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)	184.9
			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 ⁵⁵	5.2	12.2	17.9	2.8 *	167.5 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)	264.5
			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)	263.5
			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)	263.0	
		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)	(23)	(23)	(23)	265.5	
		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.

⁵: Significantly different from the control at $p \leq 0.05$ by Mann-Whitney U-test.

⁵⁵: 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	26.8	43.7	58.9	
			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.

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.

43-75-

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

Gener- ation	Group	Copulation index		Fertility index		Gestation index (Inci- dence, %)	Pre- coital interval (days)	Gesta- tion length (days)	Number of implanta- tions	Delivery index (%) ^a	Number of pups delivered	Sex ratio	Viability index (%) ^b on postnatal day			
		Male (Inci- dence, %)	Female (Inci- dence, %)	Male (Inci- dence, %)	Female (Inci- dence, %)								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				
	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				
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
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
													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				
	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				
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
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
													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.