

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

Generation	Group	Number of animals	Mean	S.D.	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)

Genes- 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)

Generation Group	Number of animals	Time for maze trials (sec)				Number of errors for maze trials													
		Day 1		Day 2		Day 3		Day 4											
		Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.										
F1 Control	10	8.2	2.4	58.0	35.1	29.0	9.8	30.9	12.1	0.0	0.1	10.2	7.2	2.8	1.8	2.8	2.0		
		8.1	1.2	47.1	20.5	23.6	7.0	19.8	7.9	0.1	0.1	8.5	2.2	3.0	1.7	0.9			
DCBS 80 ppm	10	8.9	1.9	46.3	19.6	35.1	16.1	26.7	11.8	0.1	0.1	7.8	2.9	5.1	3.9	2.6	2.2		
		8.7	2.1	58.2	23.1	30.7	11.5	27.0	7.6	0.0	0.1	10.8	4.1	4.3	2.5	2.4	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-benzothiazosulfenamide (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-Dicyclobexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

Generation	Group	Number of animals	WBC 10 ³ /μL	Differential count of WBC %						
				Neutrophil Stab form	Segmented	Eosino- phil	Baso- phil	Mono- cyte	Lympho- cyte	Others
F0	Control	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	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	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	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	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	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	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	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)

Generation	Group	Number of animals	WBC 10 ³ /μL	Differential count of WBC %						
				Stab form	Neutrophil Segmented	Eosino-phil	Baso-phil	Mono-cyte	Lympho-cyte	Others
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	

Table 24 Serum hormone levels in F0 and F1 parental male rats treated with N,N-Dicyclohexyl-2-benzothiazosulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

Generation	Group	Number of animals	Testosterone (ng/mL)	DHT ^a (pg/mL)	LH ^b (ng/mL)	FSH (ng/mL)
F0	Control	Mean	1.32	80.9	1.03	8.87
		S.D.	0.90	41.4	0.10	1.61
	DCBS 80 ppm	Mean	1.38	82.2	0.83	9.55
		S.D.	0.97	32.0	0.72	2.16
DCBS 600 ppm	Mean	1.01	69.1	1.26	9.43	
	S.D.	0.29	28.3	0.38	1.40	
DCBS 4500 ppm	Mean	1.07	56.4	1.08	9.31	
	S.D.	0.92	34.9	0.54	0.97	
F1	Control	Mean	0.40	39.2	1.38	7.68
		S.D.	0.13	26.7	0.32	1.46
	DCBS 80 ppm	Mean	0.99 ^s	49.7	1.23	7.05
		S.D.	0.70	14.6	0.56	1.02
DCBS 600 ppm	Mean	0.89	48.1	1.72 ^s	6.92	
	S.D.	0.63	21.1	0.12	1.41	
DCBS 4500 ppm	Mean	0.72	41.9	1.58	7.84	
	S.D.	0.43	25.6	0.34	1.53	

a: The actual measurement of DHT was below the lower limit of quantification (<25.0 pg/mL) in one F1 animal each in the control and 4500 ppm groups.

b: The actual measurement of LH was below the lower limit of quantification (<0.80 ng/mL) in three F0 and one F1 animals in the 80 ppm group and one F0 animal in the 4500 ppm group.

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

Table 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)

Generation	Group	Number of animals	Estradiol (pg/mL)	Progesterone (ng/mL)	LH ^a (ng/mL)	FSH (ng/mL)
F0	Control	Mean	80.5	5.17	1.30	5.75
		S.D.	15.7	3.59	0.22	0.99
	DCBS 80 ppm	Mean	66.7	8.49	1.13	6.29
		S.D.	16.2	4.37	0.27	1.14
DCBS 600 ppm	Mean	68.7	8.08	1.35	5.99	
	S.D.	16.0	4.70	0.20	1.06	
DCBS 4500 ppm	Mean	64.0	9.88	1.15	5.60	
	S.D.	12.3	4.20	0.49	0.86	
F1	Control	Mean	73.8	6.42	1.45	3.12
		S.D.	25.3	2.84	0.26	0.28
	DCBS 80 ppm	Mean	61.9	8.95	1.34	3.63
		S.D.	17.2	3.55	0.59	1.38
DCBS 600 ppm	Mean	59.7	7.20	1.52	3.91	
	S.D.	21.5	4.66	0.24	1.32	
DCBS 4500 ppm	Mean	63.5	8.59	1.55	4.50	
	S.D.	26.7	5.85	0.42	1.50	

a: The actual measurement of LH was below the lower limit of quantification (<0.80 ng/mL) in one F1 animal in the 80 ppm group and one F0 animal in the 4500 ppm group.

Table 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)

Generation	Item	DCBS (ppm)																							
		Control						80						600						4500					
		A	B	C	T	A	B	C	T	A	B	C	T	A	B	C	T	A	B	C	T				
F0	Number of animals examined	22	2	0	24	23	0	1	24	24	0	0	24	24	0	0	24	24	0	0	24				
	Number of animals with abnormal findings	0	0	-	0	0	-	1	1	1	1	3	-	3	-	-	3	1	-	-	1				
	Findings ^a																								
	Incisor: Malocclusion	0	0	-	0	0	-	1	1	1	-	-	-	1	-	-	1	0	-	-	0				
	Nasal bone: Fracture	0	0	-	0	0	-	1	1	1	0	-	-	0	-	-	0	0	-	-	0				
	Stomach, duodenum, jejunum, ileum and cecum: Retention gas	0	0	-	0	0	-	1	1	1	0	-	-	0	-	-	0	0	-	-	0				
	Ileum: White mass, serosa	0	0	-	0	0	-	0	0	0	-	-	-	1	-	-	1	0	-	-	0				
	Thickening, mucosa	0	0	-	0	0	-	0	0	0	-	-	-	1	-	-	1	0	-	-	0				
	Mesenteric lymph node: Swelling	0	0	-	0	0	-	0	0	1	-	-	-	1	-	-	1	0	-	-	0				
	Testis: Atrophy	0	0	-	0	0	-	0	0	0	-	-	-	0	-	-	0	1	-	-	1				
	Epididymis: Atrophy	0	0	-	0	0	-	0	0	0	-	-	-	0	-	-	0	1	-	-	1				
F1	Number of animals examined	23	1	0	24	22	2	0	24	20	4	0	24	24	0	0	24	24	0	0	24				
	Number of animals with abnormal findings	2	1	-	3	4	0	-	4	1	0	-	1	6	-	-	6	-	-	-	6				
	Findings ^a																								
	Incisor: Malocclusion	0	0	-	0	0	0	-	0	0	0	-	0	0	0	-	0	1	-	-	1				
	Ileum: Diverticulum	0	0	-	0	0	0	-	0	0	0	-	0	0	0	-	0	2	-	-	2				
	Kidney: Dilatation, renal pelvis	1	1	-	2	3	0	-	3	1	0	-	1	2	-	-	2	-	-	-	-				
	Fine white granule, renal pelvis	0	0	-	0	1	0	-	1	0	0	-	0	0	0	-	0	0	-	-	0				
	Seminal vesicle: Small size	0	0	-	0	1	0	-	1	0	0	-	0	0	0	-	0	1	-	-	1				
	Testis: Atrophy	1	0	-	1	0	0	-	0	0	0	-	0	0	0	-	0	0	-	-	0				
	Epididymis: Atrophy	1	0	-	1	0	0	-	0	0	0	-	0	0	0	-	0	0	-	-	0				

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

Fate: A, animals that impregnated a female; B, animals that unsuccessfully mated or did not impregnate a female; C, animals that were euthanized during the study; T, total (A+B+C).

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

-: Not applicable.

Table 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)

Generation	Item	Control												DCBS (ppm)											
		80				600				4500				600				4500							
		A	B	C	T	A	B	C	T	A	B	C	T	A	B	C	T	A	B	C	T				
F0	Number of animals examined	22	2	0	24	24	0	0	24	24	0	0	24	24	0	0	24	24	0	0	24	24	0	0	24
	Number of animals with abnormal findings	4	2	-	6	0	-	-	0*	0	-	-	0*	0	-	-	0*	1	-	-	1	-	-	-	1
	Findings ^a																								
	Skin: Subcutaneous yellowish/grayish white mass	1	0	-	1	0	-	-	0	0	-	-	0	0	-	-	0	1	-	-	1	-	-	-	1
	Incisor: Malocclusion/fracture	3	0	-	3	0	-	-	0	0	-	-	0	0	-	-	0	0	-	-	0	0	-	-	0
	Nasal bone: Deformity	1	0	-	1	0	-	-	0	0	-	-	0	0	-	-	0	0	-	-	0	0	-	-	0
	Ileum: Diverticulum	0	1	-	1	0	-	-	0	0	-	-	0	0	-	-	0	0	-	-	0	0	-	-	0
	Uterine horn: Retention, yellowish white mucous fluid	0	1	-	1	0	-	-	0	0	-	-	0	0	-	-	0	0	-	-	0	0	-	-	0
	Vagina: Atresia	0	2	-	2	0	-	-	0	0	-	-	0	0	-	-	0	0	-	-	0	0	-	-	0
F1	Number of animals examined	22	1	1	24	22	2	0	24	21	3	0	24	23	1	0	24	23	1	0	24	23	1	0	24
	Number of animals with abnormal findings	0	0	0	0	0	0	-	0	1	0	-	1	4	1	-	5*	4	1	-	5*	4	1	-	5*
	Findings ^a																								
	Incisor: Malocclusion	0	0	0	0	0	0	-	0	0	0	-	0	3	0	-	3	3	0	-	3	3	0	-	3
	Cerebrum: Dilatation, ventricle	0	0	0	0	0	0	-	0	0	0	-	0	0	0	-	0	0	0	-	0	0	0	-	0
	Thyroid: Aplasia	0	0	0	0	0	0	-	0	0	0	-	0	1	0	-	1	1	0	-	1	1	0	-	1
	Thymus: Atrophy	0	0	0	0	0	0	-	0	0	0	-	0	1	0	-	1	1	0	-	1	1	0	-	1
	Kidney: Dilatation, renal pelvis	0	0	0	0	0	0	-	0	1	0	-	1	0	0	-	0	0	0	-	0	0	0	-	0
	Ureter: Dilatation	0	0	0	0	0	0	-	0	1	0	-	1	0	0	-	0	0	0	-	0	0	0	-	0

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

Fate: A, animals that had weanlings; B, animals that were not pregnant and that did not produce viable pups or weanlings; C, animals that died during the study; T, total (A+B+C).

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

-: Not applicable.

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

Table 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)

Generation Group	Number of animals	Body weight		Brain		Pituitary gland		Thyroid ^d		Thymus		Liver		Kidney ^e		Spleen	
		g	%	g	%	mg	10 ⁻³ %	mg	10 ⁻³ %	mg	10 ⁻³ %	g	%	g	%	mg	10 ⁻³ %
F0 Control	24	Mean	624.4	2.25	0.366	12.8	2.07	24.0	3.85	300	48.2	20.45	3.25	3.64	0.585	882	142
		S.D.	76.0	0.08	0.041	1.3	0.22	4.0	0.60	73	11.3	4.34	0.33	0.42	0.043	158	20
		Mean	612.5	2.28	0.375	13.1	2.16	23.7	3.87	289	47.2	19.76	3.22	3.64	0.595	835	137
DCBS 80 ppm	23	S.D.	61.0	0.10	0.034	1.4	0.22	4.3	0.59	55	8.2	2.94	0.25	0.41	0.044	143	20
		Mean	603.4	2.25	0.376	12.9	2.15	24.4	4.08	318	52.9	19.76	3.27	3.57	0.593	846	140
		S.D.	51.2	0.07	0.031	1.3	0.21	4.1	0.81	67	11.1	2.09	0.18	0.29	0.035	167	24
DCBS 600 ppm	24	Mean	575.4 ^s	2.25	0.392 [*]	12.4	2.15	26.6	4.63 ^{**}	272	47.2	19.96	3.47 ^s	3.69	0.641 ^{**}	748 ^{**}	131
		S.D.	42.3	0.08	0.030	1.2	0.19	5.2	0.86	49	6.8	2.21	0.26	0.36	0.040	112	21
		Mean	630.7	2.26	0.363	13.6	2.17	24.9	3.95	346	54.8	20.80	3.28	3.70	0.586	909	145
F1 Control	24	S.D.	74.7	0.10	0.038	1.4	0.23	4.9	0.66	116	17.0	3.73	0.29	0.52	0.041	129	16
		Mean	605.1	2.29	0.380	13.9	2.30	23.3	3.86	269 ^s	44.5 ^s	19.69	3.25	3.66	0.606	845	139
		S.D.	47.7	0.06	0.028	1.3	0.25	4.7	0.78	54	8.9	2.32	0.19	0.23	0.042	141	18
DCBS 80 ppm	24	Mean	614.2	2.26	0.370	13.9	2.27	23.8	3.88	331	53.9	21.19	3.46	3.69	0.602	847	138
		S.D.	52.5	0.06	0.030	1.1	0.17	4.5	0.69	83	12.7	2.06	0.28	0.36	0.047	124	17
		Mean	622.6	2.21 ^s	0.356	14.0	2.26	24.6	3.95	316	50.9	22.82 ^s	3.65 ^{**}	3.91	0.629 ^{**}	869	139
DCBS 600 ppm	24	S.D.	51.8	0.09	0.027	1.6	0.26	4.9	0.67	62	9.8	3.37	0.28	0.43	0.044	162	17
		Mean	614.2	2.26	0.370	13.9	2.27	23.8	3.88	331	53.9	21.19	3.46	3.69	0.602	847	138
		S.D.	52.5	0.06	0.030	1.1	0.17	4.5	0.69	83	12.7	2.06	0.28	0.36	0.047	124	17
DCBS 4500 ppm	24	Mean	622.6	2.21 ^s	0.356	14.0	2.26	24.6	3.95	316	50.9	22.82 ^s	3.65 ^{**}	3.91	0.629 ^{**}	869	139
		S.D.	51.8	0.09	0.027	1.6	0.26	4.9	0.67	62	9.8	3.37	0.28	0.43	0.044	162	17
		Mean	614.2	2.26	0.370	13.9	2.27	23.8	3.88	331	53.9	21.19	3.46	3.69	0.602	847	138

(to be continued)

a: Values represent the total weights of the organs of both sides.

*: 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.

Table 28 (continued) 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)

Generation Group	Number of animals	Adrenal ^a		Testis ^a		Epididymis ^a		Seminal vesicle		Prostate		
		mg	10 ⁻³ %	g	%	mg	10 ⁻³ %	g	%	mg	10 ⁻³ %	
F0 Control	24	Mean	58.0	9.3	3.54	0.576	1350	219	2.31	0.376	899	145
		S.D.	9.5	1.3	0.24	0.083	105	26	0.25	0.062	189	32
DCBS 80 ppm	23	Mean	57.9	9.5	3.62	0.598	1379	228	2.28	0.376	910	149
		S.D.	7.7	1.1	0.20	0.075	74	28	0.24	0.060	150	20
DCBS 600 ppm	24	Mean	57.7	9.6	3.57	0.594	1354	225	2.27	0.376	853	142
		S.D.	7.4	1.2	0.24	0.048	113	17	0.29	0.041	234	37
DCBS 4500 ppm	24	Mean	51.0**	8.9	3.65	0.637**	1330	232	2.15	0.375	769	134
		S.D.	6.1	1.0	0.31	0.068	115	21	0.21	0.034	165	26
F1 Control	24	Mean	60.5	9.6	3.60	0.575	1348	215	2.30	0.368	838	133
		S.D.	9.8	1.5	0.35	0.062	138	24	0.23	0.047	174	24
DCBS 80 ppm	24	Mean	60.3	10.0	3.61	0.601	1342	223	2.19	0.364	812	134
		S.D.	7.1	1.0	0.27	0.073	67	21	0.28	0.054	181	28
DCBS 600 ppm	24	Mean	61.8	10.1	3.60	0.589	1327	217	2.21	0.362	822	134
		S.D.	7.2	1.3	0.27	0.066	111	22	0.22	0.039	190	29
DCBS 4500 ppm	24	Mean	61.3	9.8	3.78	0.610	1346	217	2.07**	0.333*	784	127
		S.D.	13.1	2.0	0.32	0.062	118	19	0.26	0.045	168	31

a: Values represent the total weights of the organs of both sides.

*: 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 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)

Generation	Group	Number of animals	Body weight		Brain		Pituitary gland		Thyroid ^d		Thymus		Liver		Kidney ^e		Spleen	
			g	%	mg	10 ⁻³ %	g	%	mg	10 ⁻³ %	mg	10 ⁻³ %	g	%	g	%	mg	10 ⁻³ %
F0	Control	Mean	305.9	2.04	0.670	13.8	4.51	18.8	6.19	237	77.0	13.73	4.48	2.13	0.696	632	207	
		S.D.	28.5	0.10	0.050	1.8	0.47	4.4	1.57	71	21.6	2.51	0.67	0.29	0.063	97	27	
	DCBS 80 ppm	Mean	311.6	2.12 **	0.681	15.2 *	4.87	17.7	5.67	209	67.2	13.83	4.43	2.20	0.707	582	187 *	
		S.D.	17.1	0.09	0.046	1.9	0.63	2.2	0.71	55	17.5	1.73	0.44	0.16	0.058	78	26	
DCBS 600 ppm	Mean	313.7	2.12 **	0.676	14.7	4.70	16.9	5.40	242	77.7	13.86	4.41	2.29	0.731	583	186 *		
	S.D.	17.8	0.07	0.042	2.2	0.66	3.1	0.92	57	19.8	1.84	0.47	0.23	0.068	77	22		
DCBS 4500 ppm	Mean	288.5 ‡	2.07	0.720 **	13.6	4.71	17.5	6.10	197	68.5	13.67	4.74	2.27	0.786 **	560 *	194		
	S.D.	16.2	0.07	0.045	1.8	0.60	2.2	0.86	59	20.8	1.48	0.44	0.19	0.057	79	27		
F1	Control	Mean	331.9	2.08	0.632	15.9	4.83	19.0	5.72	251	75.3	14.55	4.39	2.37	0.713	632	191	
		S.D.	32.5	0.08	0.056	2.0	0.73	3.9	0.98	69	18.4	1.66	0.28	0.30	0.046	73	18	
	DCBS 80 ppm	Mean	331.2	2.17 **	0.658	16.1	4.90	18.2	5.51	212	64.1	14.18	4.28	2.39	0.723	599	181	
		S.D.	28.5	0.08	0.056	2.4	0.79	2.7	0.70	47	14.2	2.14	0.49	0.22	0.040	63	15	
DCBS 600 ppm	Mean	331.3	2.15 *	0.651	15.8	4.78	17.7	5.35	261	79.2	14.32	4.33	2.40	0.726	609	184		
	S.D.	23.1	0.08	0.043	1.8	0.52	3.5	1.08	65	20.2	1.49	0.41	0.21	0.063	80	19		
DCBS 4500 ppm	Mean	330.2	2.08	0.633	16.1	4.89	19.4	5.89	211	64.0	15.83	4.81 ††	2.53	0.771 ††	639	194		
	S.D.	30.8	0.08	0.060	1.9	0.66	4.1	1.15	63	18.7	2.11	0.59	0.26	0.080	115	37		

a: Values represent the total weights of the organs of both sides.

*: 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.

(to be continued)

Table 29 (continued) 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)

Generation Group	Number of animals	Adrenal ^a		Ovary ^a		Uterus	
		mg	10 ⁻³ %	mg	10 ⁻³ %	mg	10 ⁻³ %
F0 Control	22	Mean	21.8	100.2	32.8	957	313
		S.D.	9.4	2.3	15.8	4.4	189
DCBS 80 ppm	24	Mean	21.2	95.4	30.7	962	310
		S.D.	6.1	2.1	11.6	3.9	186
DCBS 600 ppm	24	Mean	21.8	101.1	32.3	975	311
		S.D.	8.6	2.6	9.1	3.1	198
DCBS 4500 ppm	24	Mean	24.1 **	91.6	31.8	1024	357
		S.D.	8.1	2.7	12.4	4.1	203
F1 Control	22	Mean	21.2	110.6	33.4	927	280
		S.D.	9.7	3.2	13.0	2.9	191
DCBS 80 ppm	22	Mean	22.2	109.1	33.0	928	283
		S.D.	10.9	3.1	16.3	4.5	128
DCBS 600 ppm	21	Mean	22.2	108.5	32.8	976	295
		S.D.	9.3	3.0	12.5	3.2	185
DCBS 4500 ppm	23	Mean	23.6 *	108.2	32.8	949	288
		S.D.	8.9	3.2	13.4	3.3	192

a: Values represent the total weights of the organs of both sides.

*: 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 30 Histopathological findings in F0 and F1 parental male rats treated with N,N-Dicyclohexyl-2-benzothiazoleisulfotamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

Gener- ation	Item	Control						DCBS (ppm)									
		A			T			80			600			4500			
		A	B	T	A	B	T	A	B	T	A	B	T	A	B	T	
F0	Number of animals examined	22	2	24	0	0	0	0	0	0	0	0	0	24	0	24	
Findings in organs/tissues examined ^{a,b,c}																	
Liver: Microgranuloma																	
	Kidney: Hyaline droplet, proximal tubular epithelium	4	2	6	-	-	-	-	-	-	-	-	-	5	-	5	
	Kidney: Eosinophilic body, proximal tubular epithelium	12	2	14	-	-	-	-	-	-	-	-	-	20	-	20	
	Regeneration, tubular epithelium	5	0	5	-	-	-	-	-	-	-	-	-	1	-	1	
	Cast, hyaline	2	0	2	-	-	-	-	-	-	-	-	-	2	-	2	
	Cellular infiltration, inflammatory cell, renal pelvicy mucosa	0	1	1	-	-	-	-	-	-	-	-	-	0	-	0	
	Cyst	2	0	2	-	-	-	-	-	-	-	-	-	1	-	1	
	Testis: Atrophy, seminiferous tubule	0	0	0	-	-	-	-	-	-	-	-	-	1	-	1	
	Epididymis: Decrease, sperm	0	0	0	-	-	-	-	-	-	-	-	-	1	-	1	
	Cell debris, lumen	0	0	0	-	-	-	-	-	-	-	-	-	1	-	1	
	Prostate: Cellular infiltration, inflammatory cell	15	0	15	-	-	-	-	-	-	-	-	-	17	-	17	
	Pituitary gland: Cyst, pars distalis	1	0	1	-	-	-	-	-	-	-	-	-	0	-	0	
	Cyst, pars intermedia	1	0	1	-	-	-	-	-	-	-	-	-	0	-	0	
	Tubular hyperplasia, pars intermedia	1	0	1	-	-	-	-	-	-	-	-	-	1	-	1	
Findings in organs/tissues in which abnormal findings were grossly observed ^{a,d}																	
	Neum: Cyst, squamous cell	-	-	-	-	-	-	-	-	-	-	-	-	1(2)	-	1(2)	
	Cellular infiltration, inflammatory cell	-	-	-	-	-	-	-	-	-	-	-	-	1(2)	-	1(2)	
	Mesenteric lymph node: Hyperplasia, lymphoid	-	-	-	-	-	-	-	-	-	-	-	-	1(1)	-	1(1)	

(to be continued)

Fate: A, animals that impregnated a female; B, animals that did not impregnate a female; T, total (A+B).

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

b: Organs/tissues examined were the liver, kidneys, thymus, thyroid, spleen, adrenals, bone marrow (femur), mesenteric lymph node, Peyer's patch, testis, epididymis, seminal vesicles, coagulating glands, prostate, mammary gland and pituitary gland.

c: Statistical analyses were made between the control and 4500 ppm groups based on the total number of animals examined.

d: Values in parentheses are the number of animals examined.

-: Not applicable.

Table 30 (continued) 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)

Generation	Item	DCBS (ppm)															
		Control			80			600			4500						
		A	B	T	A	B	T	A	B	T	A	B	T				
F1	Number of animals examined	23	1	24	0	2	2	2	0	4	4	4	24	0	24	0	24
Findings in organs/tissues examined ^{a,b,c}																	
Liver: Microgranuloma																	
Kidney: Hyaline droplet, proximal tubular epithelium																	
Eosinophilic body, proximal tubular epithelium																	
Regeneration, tubular epithelium																	
Cast, hyaline																	
Mineralization, papilla																	
Dilatation, renal pelvis																	
Testis: Atrophy, seminiferous tubule																	
Epididymis: Decrease, sperm																	
Cell debris, lumen																	
Prostate: Cellular infiltration, inflammatory cell																	
Pituitary gland: Cyst, pars distalis																	
Tubular hyperplasia, pars intermedia																	

Fate: A, animals that impregnated a female; B, animals that unsuccessfully mated or did not impregnate a female; T, total (A+B).

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

b: Organs/tissues examined were the liver, kidneys, thymus, thyroids, spleen, adrenals, bone marrow (femur), mesenteric lymph node, Peyer's patch, testis, epididymis, seminal vesicles, coagulating glands, prostate, mammary gland and pituitary gland.

c: Statistical analyses were made between the control and 4500 ppm groups based on the total number of animals examined.

-: Not applicable.

Table 31 Histopathological findings in F0 and F1 parental female rats treated with N,N-Dicyclohexyl-2-benzothiazol-sulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

Generation	Item	DCBS (ppm)																							
		Control						80						600						4500					
		A	B	C	T	A	B	C	T	A	B	C	T	A	B	C	T	A	B	C	T				
F0	Number of animals examined	22	2	0	24	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	24	0	0	24
	Findings in organs/tissues examined ^{a,b,c}																								
	Liver: Microgranuloma	5	0	-	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	7	-	-	7
	Kidney: Regeneration, tubular epithelium	1	0	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-	1
	Cellular infiltration, inflammatory cell, renal pelvic mucosa	1	0	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	-	-	0
	Mineralization, renal pelvic mucosa	0	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	-	-	0
	Mineralization, cortex	0	0	-	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-	1
	Uterine horn: Cellular infiltration, inflammatory cell	0	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	-	-	0
	Vagina: Atresia	0	2	-	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	-	-	0
	Pituitary gland: Cyst, pars intermedia	1	0	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	-	-	0
	Tubular hyperplasia, pars intermedia	1	0	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-	1
	Mammary gland: Adenocarcinoma	1	0	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-	1
F1	Number of animals examined	21	2	1	24 ^e	0	2	0	2	0	2	0	2	0	4	0	4	0	4	0	4	23	1	0	24
	Findings in organs/tissues examined ^{a,b,c}																								
	Liver: Microgranuloma	11	1	0	12	-	1	-	1	-	1	-	1	-	3	-	3	-	11	-	11	1	1	-	12
	Kidney: Regeneration, tubular epithelium	1	0	-	1	-	0	-	0	-	0	-	0	-	1	-	1	-	0	-	0	0	0	-	0
	Dilatation, tubule	0	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-	1	-	1	0	0	-	0
	Cellular infiltration, inflammatory cell, renal pelvic mucosa	1	0	-	1	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	0	0	-	0
	Cellular infiltration, inflammatory cell, cortex	0	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-	1	-	1	0	0	-	0
	Mineralization, cortico-medullary junction	0	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-	1	-	1	0	0	-	0
	Cast, hyaline	0	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-	1	-	1	0	0	-	0
	Cyst	0	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-	1	-	1	0	0	-	0
	Dilatation, renal pelvis	0	0	-	0	-	0	-	0	-	0	-	0	-	1	-	1	-	0	-	0	0	0	-	0
	Thymus: Atrophy, cortex	0	0	0	0	-	0	-	0	-	0	-	0	-	0	-	0	-	1	-	1	0	0	-	0
	Pituitary gland: Cyst, pars intermedia	1	0	0	1	-	0	-	0	-	0	-	0	-	1	-	1	-	0	-	0	0	0	-	0
	Tubular hyperplasia, pars intermedia	1	0	0	1	-	0	-	0	-	0	-	0	-	0	-	0	-	0	-	0	0	0	-	0
	Findings in organs/tissues in which abnormal findings were grossly observed ^{a,d}																								
	Cerebrum: Dilatation, ventricle	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	(1)	-	-	-	-	1(1)

Fate: A, animals that had weanlings; B, animals that were not pregnant, did not produce viable pups or weanlings, or showed abnormal estrous cyclicity; C, animals that died during the study; T, total (A+B+C).
a: Values represent the number of animals that showed abnormal findings.
b: Organs/tissues examined were the liver, kidneys, thymus, thyroids, spleen, adrenals, bone marrow (femur), mesenteric lymph node, Peyer's patch, ovaries, uterus, vagina, mammary gland and pituitary gland.
c: Statistical analyses were made between the control and 4500 ppm groups based on the total number of animals examined.
d: Values in parentheses are the number of animals examined.
e: The number of animals examined on the kidney was 23 because both sides of the kidneys in one dead animal showed autolysis.
-: Not applicable.

Table 32 Number of primordial follicles in F1 parental female rats treated with N,N-Dicyclohexyl-2-benzothiazosulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

Generation	Group	Number of animals	Mean S.D.	Number of primordial follicles ^a
F1	Control	10	Mean S.D.	323.1 56.6
	DCBS 4500 ppm	10	Mean S.D.	255.4 109.1

a: Counted based on a 5% nonrandom sample (every twentieth serial section) from right ovary of each animal.