

Table 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)

Gener- ation	Group	Number of animals		Number of primordial follicles <sup>a</sup>
F1	Control	10	Mean	323.1
			S.D.	56.6
	DCBS 4500 ppm	10	Mean	255.4
			S.D.	109.1

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

Table 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)

Gener- ation	Item	Postnatal day 0			
		Control	DCBS (ppm)		
			80	600	4500
F1	Number of litters examined	22	24	24	24
	Number of pups examined	149	175	167	158
	Number of pups with abnormal findings	2 ( 0.98 )	2 ( 1.46 )	1 ( 0.42 )	1 ( 1.39 )
	Findings <sup>a</sup> Found dead	2 ( 0.98 )	2 ( 1.46 )	1 ( 0.42 )	1 ( 1.39 )
F2	Number of litters examined	23	22	21	24
	Number of pups examined	143	143	147	163
	Number of pups with abnormal findings	0 ( 0.00 )	1 ( 0.65 )	2 ( 1.55 )	8 ( 4.67 )*
	Findings <sup>a</sup> Found dead	0 ( 0.00 )	1 ( 0.65 )	2 ( 1.55 )	8 ( 4.67 )*

(to be continued)

Values in parentheses represent the means of incidences of pups with abnormal findings (% the litter is the unit evaluated).

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

\*: Significantly different from the control at  $p \leq 0.05$  by Wilcoxon rank-sum test.

Table 33 (continued-1) 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)

Gener- ation	Item	Postnatal days 1-4			
		Control	DCBS (ppm)		
			80	600	4500
F1	Number of litters examined	22	24	24	24
	Number of pups examined	147	173	166	157
	Number of pups with abnormal findings	1 ( 0.91 )	3 ( 1.40 )	8 ( 4.73 )	3 ( 1.74 )
	Findings <sup>a</sup>				
	Found dead/lost	1 ( 0.91 )	3 ( 1.40 )	8 ( 4.73 )	3 ( 1.74 )
F2	Number of litters examined	23	22	21	24
	Number of pups examined	143	142	145	155
	Number of pups with abnormal findings	6 ( 4.09 )	9 ( 4.55 )	11 ( 7.80 )	18 ( 12.56 )
	Findings <sup>a</sup>				
	Scab on auricle	0 ( 0.00 )	0 ( 0.00 )	1 ( 0.68 )	0 ( 0.00 )
	Found dead/lost	6 ( 4.09 )	9 ( 4.55 )	10 ( 7.12 )	18 ( 12.56 )

(to be continued)

Values in parentheses represent the means of incidences of pups with abnormal findings (% the litter is the unit evaluated).

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

Table 33 (continued-2) 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)

Gener- ation	Item	Postnatal days 5-21			
		Control	DCBS (ppm)		
			80	600	4500
F1	Number of litters examined	22	24	24	24
	Number of pups examined	86	98	95	97
	Number of pups with abnormal findings	0 ( 0.00 )	1 ( 1.04 )	1 ( 1.39 )	0 ( 0.00 )
	Findings <sup>a</sup>				
	Found dead/lost	0 ( 0.00 )	1 ( 1.04 )	1 ( 1.39 )	0 ( 0.00 )
F2	Number of litters examined	23	22	21	23
	Number of pups examined	87	81	81	92
	Number of pups with abnormal findings	0 ( 0.00 )	1 ( 1.14 )	2 ( 2.38 )	2 ( 2.17 )
	Findings <sup>a</sup>				
		Microphthalmia	0 ( 0.00 )	1 ( 1.14 )	0 ( 0.00 )
	Lost	0 ( 0.00 )	0 ( 0.00 )	2 ( 2.38 )	2 ( 2.17 )

(to be continued)

Values in parentheses represent the means of incidences of pups with abnormal findings (%; the litter is the unit evaluated).

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

Table 33 (continued-3) 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)

Gener- ation	Item	Postnatal days 22-26			
		Control	DCBS (ppm)		
			80	600	4500
F1	Number of litters examined	22	24	24	24
	Number of weanlings examined	86	97	94	97
	Number of weanlings with abnormal findings	0 ( 0.00 )	0 ( 0.00 )	0 ( 0.00 )	0 ( 0.00 )
F2	Number of litters examined	22	22	21	23
	Number of weanlings examined	83	81	79	90
	Number of weanlings with abnormal findings	0 ( 0.00 )	1 ( 1.14 )	0 ( 0.00 )	0 ( 0.00 )
	Findings <sup>a</sup>				
	Microphthalmia	0 ( 0.00 )	1 ( 1.14 )	0 ( 0.00 )	0 ( 0.00 )

Values in parentheses represent the means of incidences of weanlings with abnormal findings (%; the litter is the unit evaluated).

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

Table 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)

Gener- ation	Item	Postnatal day 0			
		Control	DCBS (ppm)		
			80	600	4500
F1	Number of litters examined	22	24	24	24
	Number of pups examined	133	141	163	143
	Number of pups with abnormal findings	1 ( 0.45 )	0 ( 0.00 )	0 ( 0.00 )	2 ( 1.22 )
	Findings <sup>a</sup>				
	Found dead	1 ( 0.45 )	0 ( 0.00 )	0 ( 0.00 )	2 ( 1.22 )
F2	Number of litters examined	23	22	20	24
	Number of pups examined	150	134	117	149
	Number of pups with abnormal findings	4 ( 2.42 )	0 ( 0.00 )*	2 ( 1.83 )	4 ( 2.43 )
	Findings <sup>a</sup>				
	Found dead	4 ( 2.42 )	0 ( 0.00 )*	2 ( 1.83 )	4 ( 2.43 )

(to be continued)

Values in parentheses represent the means of incidences of pups with abnormal findings (%; the litter is the unit evaluated).

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

\*: Significantly different from the control at  $p \leq 0.05$  by Wilcoxon rank-sum test.

Table 34 (continued-1) 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)

Gener- ation	Item	Postnatal days 1-4			
		Control	DCBS (ppm)		
			80	600	4500
F1	Number of litters examined	22	24	24	24
	Number of pups examined	132	141	163	141
	Number of pups with abnormal findings	4 ( 3.05 )	3 ( 1.81 )	3 ( 1.88 )	4 ( 2.22 )
	Findings <sup>a</sup>				
	Trauma and scab on forelimb	1 ( 0.76 )	0 ( 0.00 )	0 ( 0.00 )	0 ( 0.00 )
	Found dead/lost	3 ( 2.29 )	3 ( 1.81 )	3 ( 1.88 )	4 ( 2.22 )
F2	Number of litters examined	23	22	20	24
	Number of pups examined	146	134	115	145
	Number of pups with abnormal findings	8 ( 3.98 )	10 ( 7.05 )	5 ( 4.43 )	16 ( 10.68 )
	Findings <sup>a</sup>				
	Scab on hindlimb	0 ( 0.00 )	1 ( 0.76 )	0 ( 0.00 )	0 ( 0.00 )
	Found dead/lost	8 ( 3.98 )	9 ( 6.29 )	5 ( 4.43 )	16 ( 10.68 )

(to be continued)

Values in parentheses represent the means of incidences of pups with abnormal findings (%; the litter is the unit evaluated).

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

Table 34 (continued-2) 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)

Gener- ation	Item	Postnatal days 5-21			
		Control	DCBS (ppm)		
			80	600	4500
F1	Number of litters examined	22	24	24	24
	Number of pups examined	88	94	97	95
	Number of pups with abnormal findings	0 ( 0.00 )	1 ( 1.04 )	0 ( 0.00 )	1 ( 1.04 )
	Findings <sup>a</sup>				
	Found dead/lost	0 ( 0.00 )	1 ( 1.04 )	0 ( 0.00 )	1 ( 1.04 )
F2	Number of litters examined	23	22	20	23
	Number of pups examined	90	80	77	86
	Number of pups with abnormal findings	0 ( 0.00 )	0 ( 0.00 )	3 ( 4.17 )	2 ( 2.54 )
	Findings <sup>a</sup>				
	Found dead/lost	0 ( 0.00 )	0 ( 0.00 )	3 ( 4.17 )	2 ( 2.54 )

(to be continued)

Values in parentheses represent the means of incidences of pups with abnormal findings (% the litter is the unit evaluated).

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



Table 34 (continued-3) 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)

Gener- ation	Item	Postnatal days 22-26			
		Control	DCBS (ppm)		
			80	600	4500
F1	Number of litters examined	22	24	24	24
	Number of weanlings examined	88	93	97	94
	Number of weanlings with abnormal findings	0 ( 0.00 )	2 ( 2.08 )	0 ( 0.00 )	0 ( 0.00 )
	Findings <sup>a</sup>				
	Found dead	0 ( 0.00 )	2 ( 2.08 )	0 ( 0.00 )	0 ( 0.00 )
F2	Number of litters examined	22	22	20	23
	Number of weanlings examined	86	80	74	84
	Number of weanlings with abnormal findings	0 ( 0.00 )	0 ( 0.00 )	0 ( 0.00 )	0 ( 0.00 )

Values in parentheses represent the means of incidences of weanlings with abnormal findings (% the litter is the unit evaluated).

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

Table 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)

Gener- ation	Group	Number of litters		Male					Female					
				Body weight (g) on postnatal day					Body weight (g) on postnatal day					
				0	4	7	14	21	0	4	7	14	21	
F1	Control	22	Mean	6.9	11.2	18.6	37.2	62.3	6.5	10.9	18.1	36.3	60.7	
			S.D.	0.5	1.1	1.8	3.6	5.6	0.5	1.3	1.9	3.5	5.2	
	DCBS 80 ppm	24	Mean	6.7	10.5	18.1	36.8	62.2	6.3	10.1	17.1	34.8	58.5	
			S.D.	0.6	1.2	1.7	2.4	3.7	0.5	1.4	2.3	3.6	6.0	
	DCBS 600 ppm	24	Mean	6.7	10.5	17.7	36.0	60.2	6.3	10.0	17.2	35.0	58.2	
			S.D.	0.6	1.4	2.5	4.0	6.3	0.5	1.2	2.3	4.0	6.5	
	DCBS 4500 ppm	24	Mean	6.6	10.3 *	16.7 **	33.6 <sup>SS</sup>	55.3 **	6.3	9.9 *	16.2 **	32.8 **	53.7 **	
			S.D.	0.7	1.0	1.6	2.5	4.8	0.6	1.0	1.4	2.6	4.5	
	F2	Control	23	Mean	6.8	11.0	18.5	37.1	62.5	6.5	10.5	17.6	35.9	59.6
				S.D.	0.9	2.3	2.7	4.0	7.0	1.0	2.3	2.9	4.1	6.6
		DCBS 80 ppm	22	Mean	6.7	11.1	18.4	37.8	63.4	6.3	10.5	17.7	36.6	60.7
				S.D.	0.8	2.6	3.8	6.3	9.4	0.7	2.5	3.8	5.7	8.5
DCBS 600 ppm		21	Mean	6.7	10.0	17.1	35.5	60.6	(20)	(20)	(20)	(20)	(20)	
			S.D.	0.5	2.1	2.8	3.8	5.6	0.4	2.0	2.8	4.9	7.0	
DCBS 4500 ppm		24	Mean	6.7	10.0	15.9 *	32.3 **	53.5 **	6.3	9.5	15.5	31.7 *	52.0 **	
			S.D.	0.6	1.4	2.3	4.1	5.9	0.7	1.5	2.2	3.9	5.7	

Values in parentheses are the number of litters 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.

<sup>SS</sup>: Significantly different from the control at  $p \leq 0.01$  by Mann-Whitney U-test.

Table 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)

Gener- ation	Group	Number of litters		Male		Female	
				AGD (mm)	AGD/(BW) <sup>1/3</sup>	AGD (mm)	AGD/(BW) <sup>1/3</sup>
F1	Control	22	Mean	5.60	2.51	3.02	1.36
			S.D.	0.28	0.09	0.11	0.05
	DCBS 80 ppm	24	Mean	5.50	2.52	2.95	1.37
			S.D.	0.28	0.08	0.14	0.06
	DCBS 600 ppm	24	Mean	5.51	2.52	2.99	1.39
			S.D.	0.41	0.12	0.14	0.04
	DCBS 4500 ppm	24	Mean	5.54	2.55	2.96	1.38
			S.D.	0.28	0.09	0.14	0.04
F2	Control	23	Mean	5.54	2.50	2.93	1.34
			S.D.	0.51	0.12	0.19	0.04
	DCBS 80 ppm	22	Mean	5.60	2.53	2.91	1.34
			S.D.	0.55	0.14	0.22	0.06
	DCBS 600 ppm	21	Mean	5.39	2.51	2.88	1.35
			S.D.	0.56	0.12	0.19	0.03
	DCBS 4500 ppm	23	Mean	5.47	2.55	2.85	1.35
			S.D.	0.38	0.08	0.18	0.05

Values in parentheses are the number of litters examined.

AGD: Anogenital distance.

BW: Body weight.

Table 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)

Gener- ation	Group	Number of litters		Male						Female						
				Pinna detachment				Incisor eruption Age at compla- tion (days)	Eye opening Age at compla- tion (days)	Pinna detachment				Incisor eruption Age at compla- tion (days)	Eye opening Age at compla- tion (days)	
				Completion rate (%) on postnatal day						Completion rate (%) on postnatal day						
1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	
F1	Control	22	Mean	6.3	25.5	95.9	100.0	10.2	14.5	6.4	33.9	97.2	100.0	10.1	14.4	
			S.D.	18.3	35.3	11.3	0.0	0.6	0.6	21.0	38.9	7.6	0.0	0.6	0.6	
	DCBS 80 ppm	24	Mean	1.2	31.2	93.8	100.0	10.8 **	14.5	3.5	39.3	93.4	99.4	10.7 **	14.5	
			S.D.	4.0	41.7	15.1	0.0	0.6	0.5	8.6	43.4	15.7	2.9	0.7	0.7	
	DCBS 600 ppm	24	Mean	0.0	15.2	94.4	100.0	10.3	14.7	0.0	20.0	93.3	100.0	10.2	14.4	
			S.D.	0.0	22.8	20.7	0.0	0.6	0.5	0.0	32.4	21.1	0.0	0.7	0.4	
	DCBS 4500 ppm	24	Mean	5.0	23.6	99.3	100.0	10.5	14.6	4.2	27.1	99.5	100.0	10.2	14.5	
			S.D.	16.9	33.7	3.4	0.0	0.4	0.5	20.4	34.4	2.3	0.0	0.6	0.5	
	F2	Control	23	Mean	13.8	30.0	87.2	100.0	(22) 9.7	(22) 14.4	10.3	30.2	88.0	99.1	(22) 9.8	(22) 14.3
				S.D.	32.0	44.2	29.1	0.0	0.7	0.7	28.4	40.0	29.2	4.2	0.7	0.6
		DCBS 80 ppm	22	Mean	9.1	28.6	91.5	100.0	10.6 **	14.6	7.6	30.8	91.7	97.7	10.4 *	14.4
				S.D.	29.4	41.1	23.1	0.0	0.9	0.8	25.1	43.8	22.4	10.7	0.8	0.8
DCBS 600 ppm		21	Mean	3.1	26.1	86.6	100.0	9.9	14.3	(20) 0.7	(20) 26.1	(20) 91.7	(20) 100.0	(20) 10.0	(20) 14.4	
			S.D.	11.2	40.5	23.2	0.0	0.6	0.7	3.2	37.8	15.0	0.0	0.6	0.5	
DCBS 4500 ppm		24	Mean	1.7	31.7	92.4	100.0	(23) 10.3 *	(23) 14.6	(23) 3.6	(23) 40.2	(23) 92.6	(23) 100.0	(23) 10.4 *	(23) 14.5	
			S.D.	8.2	38.8	18.0	0.0	0.8	0.6	15.4	40.0	18.3	0.0	0.9	0.7	

Values in parentheses are the number of litters 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 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)

Gener- ation	Group	Number of animals	Male						Female				
			Surface righting reflex		Negative geotaxis reflex		Air righting reflex	Surface righting reflex		Negative geotaxis reflex		Air righting reflex	
			Success rate (%)	Response time (sec)	Completion ratio (%)	Response time (sec)	Success rate (%)	Success rate (%)	Response time (sec)	Completion ratio (%)	Response time (sec)	Success rate (%)	
F1	Control	22	Mean S.D.	100.0 0.0	2.1 1.6	22/22 (100.0)	14.5 8.0	100.0 0.0	100.0 0.0	2.8 3.4	22/22 (100.0)	15.3 6.8	100.0 0.0
	DCBS 80 ppm	24	Mean S.D.	100.0 0.0	1.5 0.5	24/24 (100.0)	15.4 8.2	100.0 0.0	100.0 0.0	1.6 0.6	24/24 (100.0)	14.1 6.0	100.0 0.0
	DCBS 600 ppm	24	Mean S.D.	100.0 0.0	2.4 2.3	24/24 (100.0)	13.8 6.4	100.0 0.0	100.0 0.0	1.9 0.9	24/24 (100.0)	15.4 6.2	100.0 0.0
	DCBS 4500 ppm	24	Mean S.D.	100.0 0.0	1.8 1.2	24/24 (100.0)	16.0 7.5	100.0 0.0	100.0 0.0	3.4 3.9	24/24 (100.0)	18.3 7.6	100.0 0.0
F2	Control	22	Mean S.D.	100.0 0.0	2.5 1.6	22/22 (100.0)	15.3 6.3	100.0 0.0	100.0 0.0	2.6 1.8	22/22 (100.0)	16.9 7.2	100.0 0.0
	DCBS 80 ppm	22	Mean S.D.	100.0 0.0	2.2 1.8	22/22 (100.0)	17.2 7.4	98.5 7.1	97.0 14.2	2.4 2.0	22/22 (100.0)	14.0 6.5	100.0 0.0
	DCBS 600 ppm	21	Mean S.D.	100.0 0.0	1.7 0.5	21/21 (100.0)	14.4 5.7	100.0 0.0	100.0 0.0	2.5 1.7	20/20 (100.0)	12.6 8.1	98.3 7.4
	DCBS 4500 ppm	23	Mean S.D.	100.0 0.0	2.1 1.9	23/23 (100.0)	16.1 4.9	100.0 0.0	100.0 0.0	3.2 4.5	22/23 (95.7)	16.0 6.2	100.0 0.0

Surface righting reflex, negative geotaxis reflex and air righting reflex were examined on postnatal day 5, 8 and 18, respectively.

Completion ratio (%) = (number of animals showing positive response/number of animals examined) x 100.

Values in parentheses are the number of animals examined.

Table 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)

Gener- ation	Item	Control	DCBS (ppm)			
			80	600	4500	
F1	Number of litters examined	17	23	21	21	
	Number of pups examined	62	77	67	61	
	Number of pups with abnormal findings	0 ( 0.00 )	1 ( 1.09 )	0 ( 0.00 )	0 ( 0.00 )	
	Findings <sup>a</sup>					
	Liver: Yellowish white discoloration	0 ( 0.00 )	1 ( 1.09 )	0 ( 0.00 )	0 ( 0.00 )	
F2	Number of litters examined	17	17	15	19	
	Number of pups examined	52	58	57	59	
	Number of pups with abnormal findings	2 ( 1.96 )	1 ( 1.47 )	1 ( 2.22 )	1 ( 2.63 )	
	Findings <sup>a</sup>					
		Auricle: Scab	0 ( 0.00 )	0 ( 0.00 )	1 ( 2.22 )	0 ( 0.00 )
		Digestive tract: Retention, gas	2 ( 1.96 )	1 ( 1.47 )	0 ( 0.00 )	0 ( 0.00 )
	Kidney: Dilatation, renal pelvis	0 ( 0.00 )	0 ( 0.00 )	0 ( 0.00 )	1 ( 2.63 )	

Values in parentheses represent the means of incidences of pups with abnormal findings (%; the litter is the unit evaluated).

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

Table 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)

Gener- ation	Item	Control	DCBS (ppm)			
			80	600	4500	
F1	Number of litters examined	17	18	21	17	
	Number of pups examined	44	46	64	46	
	Number of pups with abnormal findings	3 ( 7.06 )	0 ( 0.00 )	0 ( 0.00 )	0 ( 0.00 )	
	Findings <sup>a</sup>					
	Liver: Yellowish white discoloration	1 ( 2.94 )	0 ( 0.00 )	0 ( 0.00 )	0 ( 0.00 )	
	Kidney: Dilatation, renal pelvis	1 ( 1.18 )	0 ( 0.00 )	0 ( 0.00 )	0 ( 0.00 )	
	Ureter: Dilatation	1 ( 1.18 )	0 ( 0.00 )	0 ( 0.00 )	0 ( 0.00 )	
	Forelimb: Scab	1 ( 2.94 )	0 ( 0.00 )	0 ( 0.00 )	0 ( 0.00 )	
	<hr/>					
	F2	Number of litters examined	18	14	15	19
Number of pups examined		53	49	37	51	
Number of pups with abnormal findings		2 ( 11.11 )	1 ( 3.57 )	1 ( 3.33 )	1 ( 2.63 )	
Findings <sup>a</sup>						
Digestive tract: Retention, gas		1 ( 5.56 )	0 ( 0.00 )	0 ( 0.00 )	1 ( 2.63 )	
Digestive tract: Dark red contents		0 ( 0.00 )	0 ( 0.00 )	1 ( 3.33 )	0 ( 0.00 )	
Forelimb: Oligodactyly		1 ( 5.56 )	0 ( 0.00 )	0 ( 0.00 )	0 ( 0.00 )	
Hindlimb: Scab		0 ( 0.00 )	1 ( 3.57 )	0 ( 0.00 )	0 ( 0.00 )	

Values in parentheses represent the means of incidences of pups with abnormal findings (% the litter is the unit evaluated).

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

Table 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)

Gener- ation	Item	Control	DCBS (ppm)		
			80	600	4500
F1	Number of litters examined	22	24	24	24
	Number of animals examined	62	73	71	73
	Number of animals with abnormal findings	0 ( 0.00 )	1 ( 1.39 )	3 ( 4.17 )	1 ( 1.39 )
	Findings <sup>a</sup>				
	Ileum: Diverticulum	0 ( 0.00 )	1 ( 1.39 )	0 ( 0.00 )	0 ( 0.00 )
	Kidney: Dilatation, renal pelvis	0 ( 0.00 )	0 ( 0.00 )	3 ( 4.17 )	1 ( 1.39 )
F2	Number of litters examined	23	22	21	23
	Number of animals examined	87 <sup>b</sup>	81	79	90
	Number of animals with abnormal findings	2 ( 2.90 )	6 ( 6.59 )	6 ( 7.86 )	4 ( 4.35 )
	Findings <sup>a</sup>				
	Eyeball: Microphthalmia	0 ( 0.00 )	1 ( 1.14 )	0 ( 0.00 )	0 ( 0.00 )
	Kidney: Dilatation, renal pelvis	1 ( 1.45 )	5 ( 5.45 )	6 ( 7.86 )*	3 ( 3.26 )
	Testis: Small size	1 ( 1.45 )	0 ( 0.00 )	0 ( 0.00 )	1 ( 1.09 )
Epididymis: Small size	1 ( 1.45 )	0 ( 0.00 )	0 ( 0.00 )	1 ( 1.09 )	

Values in parentheses represent the means of incidences of animals with abnormal findings (%; the litter is the unit evaluated).

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

b: Including pups that were euthanized on postnatal day 5 because of maternal death.

\*: Significantly different from the control at  $p \leq 0.05$  by Wilcoxon rank-sum test.



Table 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)

Gener- ation	Item	Control	DCBS (ppm)		
			80	600	4500
F1	Number of litters examined	22	24	24	24
	Number of animals examined	64	70	73	70
	Number of animals with abnormal findings	5 ( 9.09 )	3 ( 4.51 )	0 ( 0.00 )	5 ( 7.64 )
	Findings <sup>a</sup>				
	Cerebrum: Dilatation, ventricle	0 ( 0.00 )	0 ( 0.00 )	0 ( 0.00 )	1 ( 1.39 )
	Glandular stomach: Fine dark red patch, mucosa, multifocal	0 ( 0.00 )	1 ( 1.39 )	0 ( 0.00 )	0 ( 0.00 )
	Ileum: Diverticulum	1 ( 1.52 )	0 ( 0.00 )	0 ( 0.00 )	0 ( 0.00 )
	Kidney: Dilatation, renal pelvis	4 ( 7.58 )	2 ( 3.13 )	0 ( 0.00 )	4 ( 6.25 )
	Urinary bladder: Dark red contents	0 ( 0.00 )	1 ( 1.39 )	0 ( 0.00 )	0 ( 0.00 )
	F2	Number of litters examined	23	22	20
Number of animals examined		90 <sup>b</sup>	80	74	85
Number of animals with abnormal findings		0 ( 0.00 )	1 ( 1.14 )	6 ( 7.50 )*	2 ( 2.32 )
Findings <sup>a</sup>					
Ileum: Diverticulum		0 ( 0.00 )	0 ( 0.00 )	2 ( 2.50 )	0 ( 0.00 )
Digestive tract: Retention, gas		0 ( 0.00 )	0 ( 0.00 )	0 ( 0.00 )	1 ( 1.45 )
Kidney: Dilatation, renal pelvis	0 ( 0.00 )	1 ( 1.14 )	4 ( 5.00 )	1 ( 0.87 )	

Values in parentheses represent the means of incidences of animals with abnormal findings (%; the litter is the unit evaluated).

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

b: Including pups that were euthanized on postnatal day 5 because of maternal death.

\*: Significantly different from the control at  $p \leq 0.05$  by Wilcoxon rank-sum test.

Table 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)

Generation	Group	Number of animals		Body weight	Brain		Thymus		Liver		Kidney <sup>a</sup>		Spleen		
					g	g	%	mg	10 <sup>-3</sup> %	g	%	g	%	mg	10 <sup>-3</sup> %
F1	Control	22	Mean	92.2	1.69	1.84	359	388	4.16	4.51	1.023	1.110	394	425	
			S.D.	8.0	0.07	0.13	68	52	0.49	0.26	0.111	0.073	68	52	
	DCBS 80 ppm	24	Mean	88.9	1.69	1.91	350	393	4.09	4.60	1.040	1.171 *	352	395	
			S.D.	6.2	0.05	0.13	53	50	0.37	0.25	0.079	0.064	68	63	
	DCBS 600 ppm	24	Mean	88.1	1.70	1.94	365	416	4.09	4.64 <sup>s</sup>	1.003	1.137	356	405	
			S.D.	9.1	0.08	0.15	52	61	0.44	0.15	0.135	0.079	61	59	
	DCBS 4500 ppm	24	Mean	78.2 **	1.63 **	2.09 **	278 <sup>ss</sup>	357	3.83 *	4.89 <sup>ss</sup>	0.894 <sup>ss</sup>	1.146	278 **	357 **	
			S.D.	7.2	0.07	0.17	37	48	0.51	0.28	0.069	0.073	41	48	
	F2	Control	22	Mean	90.8	1.67	1.85	355	392	4.08	4.49	1.006	1.109	383	422
				S.D.	8.7	0.08	0.14	56	58	0.47	0.23	0.102	0.037	61	49
		DCBS 80 ppm	22	Mean	91.4	1.69	1.87	325	355	4.12	4.50	1.009	1.105	350 <sup>s</sup>	381 *
				S.D.	13.1	0.09	0.22	64	47	0.66	0.26	0.147	0.066	83	53
DCBS 600 ppm		21	Mean	89.1	1.70	1.92	361	406	4.21	4.72 <sup>ss</sup>	1.022	1.146 <sup>s</sup>	356	400	
			S.D.	6.5	0.08	0.13	47	48	0.44	0.27	0.089	0.049	46	50	
DCBS 4500 ppm		23	Mean	80.0 <sup>ss</sup>	1.63	2.05 **	283 **	354 *	3.74	4.66 <sup>ss</sup>	0.923	1.152 <sup>s</sup>	286 <sup>ss</sup>	357 **	
			S.D.	7.8	0.09	0.18	52	55	0.54	0.42	0.133	0.117	52	54	

(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.

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

<sup>ss</sup>: Significantly different from the control at  $p \leq 0.01$  by Mann-Whitney U-test.

Table 43 (continued) 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)

Gener- ation	Group	Number of animals		Adrenal <sup>a</sup>		Testis <sup>a</sup>		Epididymis <sup>a</sup>		Prostate	
				mg	10 <sup>-3</sup> %	mg	10 <sup>-3</sup> %	mg	10 <sup>-3</sup> %	mg	10 <sup>-3</sup> %
F1	Control	22	Mean	25.5	27.8	561	608	78.6	85.5	49.2	53.3
			S.D.	2.6	2.9	77	61	9.4	9.8	9.8	9.1
	DCBS 80 ppm	24	Mean	25.5	28.7	542	610	77.3	86.9	47.5	53.4
			S.D.	3.3	3.0	64	55	9.5	8.4	7.8	7.8
	DCBS 600 ppm	24	Mean	25.0	28.4	541	612	75.9	86.4	43.7	49.6
			S.D.	3.3	3.1	88	58	11.6	11.3	10.1	10.7
	DCBS 4500 ppm	24	Mean	22.4 **	28.8	529	677 <sup>55</sup>	71.3 *	91.3	42.3 *	54.0
			S.D.	2.9	4.0	88	95	10.2	11.7	8.9	9.5
F2	Control	22	Mean	25.5	28.1	548	602	79.5	87.6	50.9	55.6
			S.D.	2.8	2.8	106	89	12.5	10.6	16.6	15.0
	DCBS 80 ppm	22	Mean	24.1	26.5	516	563	72.9	80.4	44.6	48.9
			S.D.	3.4	2.6	103	69	12.3	12.6	10.4	9.9
	DCBS 600 ppm	21	Mean	24.2	27.2	528	590	72.7	81.7	47.0	52.7
			S.D.	3.8	4.3	82	65	10.0	10.6	10.3	10.1
	DCBS 4500 ppm	23	Mean	22.7 *	28.5	525	653	71.3	89.0	42.6	52.9
			S.D.	3.4	4.2	98	91	11.2	10.0	12.2	13.1

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.

<sup>55</sup>: Significantly different from the control at  $p \leq 0.01$  by Mann-Whitney U-test.

Table 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)

Generation	Group	Number of animals		Body weight	Brain		Thymus		Liver		Kidney <sup>a</sup>		Spleen		
				g	g	%	mg	10 <sup>-3</sup> %	g	%	g	%	mg	10 <sup>-3</sup> %	
F1	Control	22	Mean	85.9	1.62	1.90	361	418	3.72	4.33	0.954	1.110	338	392	
			S.D.	7.8	0.07	0.14	77	65	0.44	0.34	0.108	0.068	58	43	
	DCBS 80 ppm	24	Mean	82.5	1.65	2.01	327	398	3.52	4.27	0.967	1.173 **	323	392	
			S.D.	6.4	0.05	0.17	49	60	0.35	0.22	0.081	0.055	47	54	
	DCBS 600 ppm	24	Mean	82.8	1.64	2.00	350	423	3.65	4.41	0.940	1.133	316	382	
			S.D.	7.2	0.05	0.16	60	63	0.40	0.29	0.114	0.065	53	55	
	DCBS 4500 ppm	24	Mean	74.3 **	1.57 **	2.13 **	281 <sup>SS</sup>	379	3.43 *	4.62 **	0.850 **	1.148	249 <sup>SS</sup>	337 **	
			S.D.	6.7	0.05	0.16	43	56	0.40	0.31	0.082	0.088	32	49	
	F2	Control	22	Mean	83.6	1.62	1.96	364	439	3.71	4.44	0.915	1.096	340	407
				S.D.	9.5	0.08	0.20	50	63	0.47	0.18	0.093	0.046	63	58
		DCBS 80 ppm	22	Mean	87.2	1.66	1.92	326	373 **	3.87	4.44	0.983	1.129	331	380
				S.D.	10.8	0.07	0.19	66	56	0.50	0.23	0.137	0.085	55	46
DCBS 600 ppm		20	Mean	82.4	1.66	2.03	348	424	3.80	4.61 *	0.960	1.164 <sup>SS</sup>	320	389	
			S.D.	6.5	0.05	0.16	68	80	0.37	0.19	0.111	0.083	46	56	
DCBS 4500 ppm		23	Mean	74.6 **	1.57 *	2.11 *	283 **	379 **	3.57	4.78 **	0.885	1.187 <sup>SS</sup>	274 **	370	
			S.D.	7.9	0.07	0.18	56	63	0.46	0.26	0.101	0.061	40	52	

(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.

<sup>SS</sup>: Significantly different from the control at  $p \leq 0.01$  by Mann-Whitney U-test.

Table 44 (continued) Absolute and relative organ weights in F1 and F2 female rat wearlings treated with N,N-Dicyclohexyl-2-benzothiazolesulfenamide (DCBS) in the two-generation reproductive toxicity study (SR05241)

Gener- ation	Group	Number of animals		Adrenal <sup>a</sup>		Ovary <sup>a</sup>		Uterus		
				mg	10 <sup>-3</sup> %	mg	10 <sup>-3</sup> %	mg	10 <sup>-3</sup> %	
F1	Control	22	Mean	23.8	27.8	23.2	27.1	58.2	67.9	
			S.D.	2.6	2.8	3.3	3.3	14.5	15.8	
	DCBS 80 ppm	24	Mean	24.5	29.8	22.2	27.0	55.8	67.9	
			S.D.	2.7	3.6	3.4	4.0	7.6	9.9	
	DCBS 600 ppm	24	Mean	23.1	27.9	20.5 *	24.8	62.1	75.2	
			S.D.	2.9	2.6	3.2	4.3	12.3	14.1	
	DCBS 4500 ppm	24	Mean	21.5 *	29.1	20.3 *	27.5	48.4 <sup>§</sup>	65.0	
			S.D.	2.4	3.6	3.2	4.7	11.8	14.1	
	F2	Control	22	Mean	23.6	28.4	22.0	26.6	61.8	73.3
				S.D.	2.9	3.3	3.9	5.2	18.9	17.2
		DCBS 80 ppm	22	Mean	23.3	26.7	22.5	26.0	58.1	67.0
				S.D.	4.0	3.3	2.8	3.0	11.9	13.5
DCBS 600 ppm		20	Mean	22.2	27.0	20.9	25.5	50.0 <sup>§</sup>	60.7 *	
			S.D.	3.3	4.0	3.1	4.4	10.0	11.5	
DCBS 4500 ppm		23	Mean	21.6	29.0	21.4	29.0	46.6 <sup>§§</sup>	62.3 *	
			S.D.	3.0	3.9	2.9	4.3	12.9	15.0	

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.

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

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

Table 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)

Gener- ation	Item	Male		Female	
		Control	DCBS 4500 ppm	Control	DCBS 4500 ppm
F1	Number of weanlings examined <sup>a</sup>	22	24	22	24
	Number of weanlings with abnormal findings	0	0	0	0
F2	Number of weanlings examined <sup>a</sup>	22	23	22	23
	Number of weanlings with abnormal findings	0	0	0	0

a: Weanlings were examined on the liver, spleen and thymus in the control and DCBS 4500 ppm groups.