

Table 34 (continued-3) General appearance in F1 and F2 female rat pups and weanlings during postnatal days 0-26 treated with 1,2,5,6,9,10-hexabromocyclododecane (HBCD) in the two-generation reproductive toxicity study (SR04222)

Gener- ation	Item	Postnatal days 22-26			
		Control	HBCD (ppm)		
			150	1500	15000
F1	Number of litters examined	23	21	20	17
	Number of weanlings examined	88	85	73	55
	Number of weanlings with abnormal findings	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
F2	Number of litters examined	21	22	20	13
	Number of weanlings examined	69	78	62	36
	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).

Table 35 Body weights of F1 and F2 rat pups treated with 1,2,5,6,9,10-hexabromocyclododecane (HBCD) in the two-generation reproductive toxicity study (SR04222)

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
						(23)	(23)	(23)	(23)	(23)	(23)	(23)	(23)
F1	Control	24	Mean	6.8	10.2	16.4	36.1	61.1	6.3	9.6	15.4	33.5	56.5
			S.D.	0.5	1.7	3.1	4.8	7.1	0.5	1.4	2.8	5.3	8.0
	HBCD 150 ppm	21	Mean	6.9	10.7	17.5	36.3	62.3	6.6	10.3	17.0	35.5	59.9
			S.D.	0.6	1.8	2.4	3.6	6.5	0.7	1.8	2.5	3.6	6.4
	HBCD 1500 ppm	20	Mean	7.2	10.8	16.9	36.1	61.9	6.8 *	10.4	16.9	35.7	60.5
			S.D.	0.7	1.6	2.2	3.9	6.5	0.6	1.5	2.3	3.6	5.9
	HBCD 15000 ppm	18	Mean	6.8	9.5	15.6	33.5	55.4 *	6.5	9.2	15.1	32.6	53.2
			S.D.	0.6	1.8	2.0	2.6	4.0	0.7	1.6	1.6	3.0	4.7
						(17)	(17)	(17)			(17)	(17)	(17)
F2	Control	23	Mean	6.8	9.1	14.7	31.4	53.0	6.5	8.9	14.3	31.2	52.0
			S.D.	0.8	2.3	3.9	8.0	12.6	0.8	2.3	3.5	6.5	10.0
	HBCD 150 ppm	23	Mean	6.7	9.3	15.4	33.8	56.2	6.3	8.5	14.2	31.3	52.8
			S.D.	0.7	1.3	2.8	5.0	6.7	0.6	1.3	2.8	5.1	6.6
	HBCD 1500 ppm	20	Mean	7.1	9.0	14.3	31.0	54.1	6.7	8.8	13.5	29.3	51.2
			S.D.	0.6	1.8	3.6	7.2	10.1	0.6	1.8	3.9	7.3	10.8
	HBCD 15000 ppm	21	Mean	6.6	8.0	11.5 *	24.2 **	42.6 ^{ss}	6.2	7.3 ^{ss}	10.7 **	23.9 **	41.6 **
			S.D.	0.6	1.3	2.9	6.6	8.3	0.6	1.3	2.6	5.9	8.4

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.

^{ss}: 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 1,2,5,6,9,10-hexabromocyclododecane (HBCD) in the two-generation reproductive toxicity study (SR04222)

Generation	Group	Number of litters		Male		Female		
				AGD (mm)	AGD/(BW) ^{1/3}	AGD (mm)	AGD/(BW) ^{1/3}	
F1	Control	24	Mean	5.37	2.49	(23)	(23)	
			S.D.	0.41	0.11	2.60	1.22	
	HBCD 150 ppm	21	Mean	5.44	2.48	2.67	1.23	
			S.D.	0.36	0.10	0.16	0.06	
	HBCD 1500 ppm	20	Mean	5.38	2.44	2.62	1.20	
			S.D.	0.32	0.12	0.18	0.06	
	HBCD 15000 ppm	18	Mean	5.20	2.46	2.57	1.23	
			S.D.	0.51	0.14	0.23	0.06	
	F2	Control	22	Mean	5.12	2.46	2.69	1.30
				S.D.	0.54	0.12	0.30	0.07
		HBCD 150 ppm	22	Mean	5.12	2.44	2.71	1.33
				S.D.	0.41	0.13	0.24	0.09
HBCD 1500 ppm		20	Mean	5.04	2.43	2.71	1.32	
			S.D.	0.42	0.08	0.29	0.09	
HBCD 15000 ppm		20	Mean	(19)	(19)	2.54	1.32	
			S.D.	4.84	2.42	0.21	0.06	

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 1,2,5,6,9,10-hexabromocyclododecane (HBCD) in the two-generation reproductive toxicity study (SR04222)

Gener- ation	Group	Number of litters		Male			Female		
				Pinna detachment (%)	Incisor eruption (%)	Eye opening (%)	Pinna detachment (%)	Incisor eruption (%)	Eye opening (%)
F1	Control	24	Mean	86.0	(23) 91.6	(23) 48.2	(23) 85.8	(23) 94.9	(23) 49.3
			S.D.	26.5	17.6	41.5	29.5	11.4	37.8
	HBGD 150 ppm	21	Mean	92.5	96.4	56.7	94.7	95.2	66.7
			S.D.	16.5	12.0	37.9	14.7	10.1	41.3
	HBCD 1500 ppm	20	Mean	93.6	92.1	77.1 *	97.3	92.5	82.9 **
			S.D.	15.7	17.0	36.3	7.5	20.0	33.5
	HBCD 15000 ppm	18	Mean	81.3	(17) 89.7	(17) 45.8	86.4	92.2	54.9
			S.D.	27.9	19.9	34.6	23.8	15.4	41.4
F2	Control	23	Mean	(22) 79.9	(22) 86.4	(22) 72.7	(21) 73.6	(21) 85.7	(21) 82.9
			S.D.	36.4	25.3	40.0	39.6	26.9	26.8
	HBGD 150 ppm	22	Mean	90.5	92.8	62.5	90.6	90.9	72.7
			S.D.	22.8	19.6	40.6	22.8	26.2	37.7
	HBCD 1500 ppm	20	Mean	(18) 82.1	(18) 97.2	(18) 47.2	81.5	97.5	53.8 *
			S.D.	29.8	11.8	44.8	31.1	11.2	40.3
	HBCD 15000 ppm	21	Mean	(20) 70.1	(14) 86.3	(14) 33.9 **	66.8	(15) 90.0	(13) 48.1 *
			S.D.	39.2	27.7	34.7	40.9	28.0	42.0

Pinna detachment, incisor eruption and eye opening were observed on postnatal day 3, 11 and 14, respectively.

Values in parentheses are the number of litters examined.

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

**: Significantly different from the control at $p \leq 0.01$ by Wilcoxon rank-sum test.

Table 38 Reflex response tests in F1 and F2 rat pups treated with 1,2,5,6,9,10-hexabromocyclododecane (HBCD) in the two-generation reproductive toxicity study (SR04222)

Generation	Group	Number of animals	Male						Female					
			Surface righting reflex		Negative geotaxis reflex		Mid-air righting reflex	Surface righting reflex		Negative geotaxis reflex		Mid-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	24	Mean	100.0	2.3	24/24	17.7	100.0	100.0	3.1	23/23	13.9	100.0	
			S.D.	0.0	1.1	(100.0)	7.1	0.0	0.0	1.8	(100.0)	6.2	0.0	
								(23)	(23)	(23)		(23)	(23)	
	HBCD 150 ppm	21	Mean	100.0	2.0	21/21	16.8	100.0	100.0	2.4	21/21	11.5	100.0	
			S.D.	0.0	0.6	(100.0)	8.0	0.0	0.0	1.5	(100.0)	6.2	0.0	
	HBCD 1500 ppm	20	Mean	100.0	1.8	20/20	15.2	100.0	100.0	2.9	20/20	12.7	100.0	
			S.D.	0.0	0.5	(100.0)	7.8	0.0	0.0	2.6	(100.0)	6.3	0.0	
	HBCD 15000 ppm	17	Mean	100.0	1.6 ^{ss}	17/17	19.4	100.0	100.0	2.6	17/17	17.0	100.0	
			S.D.	0.0	0.3	(100.0)	5.9	0.0	0.0	2.6	(100.0)	6.9	0.0	
F2	Control	22	Mean	100.0	2.1	22/22	17.3	100.0	100.0	2.3	21/21	12.4	100.0	
			S.D.	0.0	1.7	(100.0)	8.6	0.0	0.0	0.9	(100.0)	5.3	0.0	
							(21)					(21)	(21)	
	HBCD 150 ppm	22	Mean	100.0	2.0	21/22	14.7	100.0	100.0	2.4	22/22	12.0	100.0	
			S.D.	0.0	1.5	(95.5)	6.8	0.0	0.0	1.7	(100.0)	5.2	0.0	
	HBCD 1500 ppm	20	Mean	100.0	2.8	19/19	15.2	98.2	100.0	2.1	20/20	16.7	95.0	
			S.D.	0.0	2.5	(100.0)	6.4	7.8	0.0	0.9	(100.0)	6.4	16.3	
	HBCD 15000 ppm	19	Mean	100.0	2.2	13/16	14.1	100.0	88.9	3.7	15/17	14.6	79.5*	
			S.D.	0.0	2.3	(81.3)	6.7	0.0	32.3	3.7	(88.2)	6.6	39.8	

Surface righting reflex, negative geotaxis reflex and mid-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.

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

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

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 1,2,5,6,9,10-hexabromocyclododecane (HBCD) in the two-generation reproductive toxicity study (SR04222)

Gener- ation	Item	Control	HBCD (ppm)		
			150	1500	15000
F1	Number of litters examined	19	19	16	16
	Number of pups examined	60	50	37	63 ^b
	Number of pups with abnormal findings	0 (0.00)	1 (1.32)	1 (1.25)	2 (4.17)
	Findings ^a				
	Lung: White mass	0 (0.00)	0 (0.00)	0 (0.00)	1 (2.08)
	Liver: Fine yellowish white patch, multifocal	0 (0.00)	0 (0.00)	0 (0.00)	1 (2.08)
	Kidney: Dilatation, renal pelvis	0 (0.00)	0 (0.00)	1 (1.25)	0 (0.00)
	External: Rudimentary tail	0 (0.00)	1 (1.32)	0 (0.00)	0 (0.00)
F2	Number of litters examined	19	21	17	17
	Number of pups examined	66	67	58 ^c	40
	Number of pups with abnormal findings	1 (2.63)	1 (1.59)	3 (3.43)	1 (1.96)
	Findings ^a				
	Liver: Yellowish white discoloration	0 (0.00)	0 (0.00)	0 (0.00)	1 (1.96)
Digestive tract: Retention, gas	1 (2.63)	1 (1.59)	3 (3.43)	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.

b: Including pups that were euthanized because of maternal death during delivery.

c: Including one animal that was not distinguished its sex because of maternal cannibalism.

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 1,2,5,6,9,10-hexabromocyclododecane (HBCD) in the two-generation reproductive toxicity study (SR04222)

Gener- ation	Item	Control	HBCD (ppm)		
			150	1500	15000
F1	Number of litters examined	21	19	18	12
	Number of pups examined	57	61	70	43 ^b
	Number of pups with abnormal findings	1 (1.19)	3 (3.38)	2 (3.70)	3 (7.92)
	Findings ^a				
	Liver: Yellowish brown discoloration	1 (1.19)	0 (0.00)	0 (0.00)	0 (0.00)
	Dark red mass, multifocal	0 (0.00)	1 (0.88)	0 (0.00)	0 (0.00)
	Jejunum: Obliteration	0 (0.00)	0 (0.00)	0 (0.00)	1 (4.17)
	Kidney: Dilatation, renal pelvis	0 (0.00)	2 (2.51)	2 (3.70)	1 (2.08)
	Abdominal cavity: Ascites	0 (0.00)	0 (0.00)	0 (0.00)	1 (4.17)
	External: Kinked tail	0 (0.00)	0 (0.00)	0 (0.00)	1 (1.67)
F2	Number of litters examined	18	22	13	18
	Number of pups examined	48	68	43	55
	Number of pups with abnormal findings	3 (4.17)	4 (6.44)	2 (5.77)	0 (0.00)
	Findings ^a				
	Digestive tract: Retention, gas	2 (2.78)	4 (6.44)	2 (5.77)	0 (0.00)
Kidney: Dilatation, renal pelvis	1 (1.39)	0 (0.00)	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.

b: Including pups that were euthanized because of maternal death during delivery.

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 1,2,5,6,9,10-hexabromocyclododecane (HBCD) in the two-generation reproductive toxicity study (SR04222)

Gener- ation	Item	HBCD (ppm)				
		Control	150	1500	15000	
F1	Number of litters examined	24	21	20	17	
	Number of animals examined	72	57	51	51	
	Number of animals with abnormal findings	3 (4.17)	2 (3.17)	7 (12.50)	11 (22.16) *	
	Findings ^a					
	Ileum: Diverticulum	0 (0.00)	0 (0.00)	1 (1.67)	0 (0.00)	
	Kidney: Dilatation, renal pelvis	3 (4.17)	2 (3.17)	6 (10.83)	11 (22.16) *	
	<hr/>					
	F2	Number of litters examined	22	22	19	16
		Number of animals examined	75	81	64	52
		Number of animals with abnormal findings	1 (1.14)	2 (2.27)	4 (5.26)	3 (4.69)
Findings ^a						
Eyeball: Swelling		0 (0.00)	0 (0.00)	1 (1.32)	1 (1.56)	
Opacity		0 (0.00)	0 (0.00)	0 (0.00)	1 (1.56)	
Kidney: Dilatation, renal pelvis		0 (0.00)	2 (2.27)	0 (0.00)	0 (0.00)	

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.

*: 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 1,2,5,6,9,10-hexabromocyclododecane (HBCD) in the two-generation reproductive toxicity study (SR04222)

Generation	Item	Control	HBCD (ppm)		
			150	1500	15000
F1	Number of litters examined	23	21	20	14
	Number of animals examined	67	63	57	35
	Number of animals with abnormal findings	0 (0.00)	2 (3.17)	0 (0.00)	3 (7.14)
	Findings ^a				
	Spleen: Hypertrophy	0 (0.00)	1 (1.59)	0 (0.00)	0 (0.00)
	Kidney: Dilatation, renal pelvis	0 (0.00)	1 (1.59)	0 (0.00)	3 (7.14)
F2	Number of litters examined	22	22	20	19
	Number of animals examined	78	81	71	53
	Number of animals with abnormal findings	2 (2.27)	1 (1.14)	2 (2.50)	0 (0.00)
	Findings ^a				
	Ileum: Diverticulum	1 (1.14)	1 (1.14)	0 (0.00)	0 (0.00)
	Kidney: Dilatation, renal pelvis	1 (1.14)	0 (0.00)	2 (2.50)	0 (0.00)

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.

Table 43 Absolute and relative organ weights in F1 and F2 male rat weanlings treated with 1,2,5,6,9,10-hexabromocyclododecane (HBCD) in the two-generation reproductive toxicity study (SR04222)

Gener- ation	Group	Number of animals		Body weight		Brain			Thymus		Liver		Kidney ^a		Spleen	
				g	g	g	%	mg	10 ⁻³ %	g	%	mg	10 ⁻³ %	mg	10 ⁻³ %	
F1	Control	23	Mean	85.7	1.64	1.94	342	398	3.94	4.60	996	1165	336	394		
			S.D.	10.9	0.09	0.19	68	55	0.63	0.37	125	74	62	64		
	HBCD 150 ppm	21	Mean	89.6	1.66	1.87	339	379	4.12	4.60	1035	1155	327	366		
			S.D.	8.1	0.05	0.17	50	45	0.48	0.32	131	92	41	42		
	HBCD 1500 ppm	20	Mean	87.7	1.62	1.86	369	421	4.43 *	5.05 **	1004	1146	334	383		
			S.D.	9.2	0.07	0.18	59	55	0.59	0.32	109	70	43	46		
	HBCD 15000 ppm	17	Mean	78.3 *	1.55 ^{ss}	1.99	317	405	4.71 **	6.00 **	894 *	1140	309	395		
			S.D.	5.8	0.06	0.13	57	70	0.58	0.44	99	78	69	81		
	F2	Control	22	Mean	82.2	1.62	2.08	343	414	3.87	4.72	965	1201	360	443	
				S.D.	17.1	0.13	0.58	92	97	0.90	0.59	167	173	83	77	
		HBCD 150 ppm	22	Mean	84.6	1.65	1.96	336	397	4.02	4.74	958	1134 ^{ss}	361	429	
				S.D.	8.7	0.08	0.16	57	54	0.55	0.35	99	56	54	64	
HBCD 1500 ppm		18	Mean	81.3	1.60	2.01	360	441	4.12	5.04 ^s	933	1155	346	426		
			S.D.	13.4	0.10	0.29	88	69	0.83	0.40	135	85	78	69		
HBCD 15000 ppm		13	Mean	64.7 ^{ss}	1.46 **	2.31 ^{ss}	282	434	3.88	6.00 ^{ss}	749 **	1170	263 **	411		
			S.D.	11.2	0.09	0.33	71	81	0.68	0.25	100	96	50	66		

(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.

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