

Table 2-2 General signs of female rats in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group	mg/kg	Number of females and general signs	Days of administration																								Total ^{a)}		
			15 [*]		16		17		18		19		20		21		22		23		24		25		26			27	
			Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post		Pre	Post
Control	0	Number of females	12	12	10	10	8	8	3	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	12	
		Normal	12	12	10	10	8	8	3	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	45	Number of females	12	12	8	8	5	5	4	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	12	
		Normal	12	12	8	8	5	5	4	4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
bisbenzene	180	Number of females	12	12	9	9	4	4	3	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	12	
		Normal	12	0	9	6	4	2	3	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	0	
	Salivation	0	12	0	3	0	2	0	2	0	1	0	1	0	1	0	1	0	1	0	1	0	1	0	1	0	2	12	
	Number of females	11	11	7	7	5	5	3	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	12	
	Normal	11	0	7	0	5	0	3	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	Salivation	0	11	0	7	0	5	0	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	12	
	Soiled hair	0	0	0	0	0	0	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4	
Hypothermia	0	0	0	0	0	0	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1		
Decrease in locomotor activity	0	0	0	0	0	0	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1		
Death	0	0	0	0	0	0	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1		

Pre: Before administration, Post: after administration.

*: Start of pairing.

a): Number of females showing abnormal signs at least once between Days 1 and 27 of administration.

Table 3-1 General signs of dams during pregnancy in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group	mg/kg	Number of dams and general signs	Days of pregnancy																													
			0		1		2		3		4		5		6		7		8		9		10		11		12		13		14	
			Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Control	0	Number of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11		
		Normal	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	45	Number of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12		
		Normal	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12		
	180	Number of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11		
		Normal	11	3	11	8	11	6	11	6	11	7	11	6	11	6	11	6	11	7	11	6	11	7	11	7	11	6	11	7	11	
	720	Salivation	0	8	0	3	0	5	0	5	0	4	0	5	0	5	0	5	0	4	0	5	0	4	0	4	0	4	0	5		
		Soiled hair	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
720	Number of dams	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10			
	Normal	9	1	10	2	10	0	10	0	10	0	10	0	10	0	10	0	10	2	10	0	10	0	10	0	10	0	10	0	10		
	Salivation	0	9	0	8	0	10	0	10	0	10	0	10	0	10	0	10	0	8	0	10	0	10	0	10	0	10	0	10	0		

Pre: Before administration, Post: after administration.

Table 3-2 General signs of dams during pregnancy in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group	mg/kg	Number of dams and general signs	Days of pregnancy																		Total ^{a)}			
			15		16		17		18		19		20		21		22		23			24		25
			Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post		Pre	Post	
Control	0	Number of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	1	1	0	0	0	0	0	11
		Normal	11	11	11	11	11	11	11	11	11	11	11	11	11	11	1	1	-	-	-	-	-	-
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	45	Number of dams	12	12	12	12	12	12	12	12	12	12	12	11	11	2	2	0	0	0	0	0	12	
		Normal	12	12	12	12	12	12	12	12	12	12	12	11	11	2	2	-	-	-	-	-	-	
	180	Number of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	0	0	0	0	0	0	0	11	
		Normal	11	10	11	10	11	10	11	8	11	8	11	9	11	9	-	-	-	-	-	-	-	
	Salivation	0	1	0	1	0	1	0	3	0	3	0	2	0	2	-	-	-	-	-	-	-		
	Soiled hair	0	1	0	1	0	1	0	3	0	3	0	2	0	2	-	-	-	-	-	-	-		
	720	Number of dams	10	10	10	10	10	10	10	10	10	10	10	10	10	5	5	0	0	0	0	0	10	
		Normal	10	0	10	0	10	1	10	0	10	0	10	1	10	2	5	0	-	-	-	-	-	
		Salivation	0	10	0	10	0	9	0	10	0	10	0	9	0	8	0	5	-	-	-	-	-	
		Soiled hair	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	-	-	-	-	-	1	

Pre: Before administration, Post: after administration.

a): Number of dams showing abnormal signs at least once between Days 0 and 25 of pregnancy.

Table 4 General signs of dams during lactation in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group	mg/kg	Number of dams and general signs	Days of lactation														Total ^{a)}				
			0		1		2		3		4		5		6			7			
			Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post					
Control	0	Number of dams	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11		
		Normal	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	-	
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	45	Number of dams	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
		Normal	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	-
	180	Number of dams	11	11	11	11	11	11	11	11	11	10	10	10	10	10	10	10	10	10	11
		Normal	11	10	11	8	11	10	11	8	11	7	10	9	10	10	10	10	10	10	-
		Salivation	0	1	0	3	0	1	0	3	0	3	0	1	0	0	0	0	0	0	4
	720	Number of dams	10	10	10	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	10
Normal		10	0	10	0	9	1	9	0	9	2	9	2	9	0	9	0	9	9	-	
Salivation		0	10	0	9	0	8	0	9	0	7	0	7	0	9	0	9	0	0	10	

Pre: Before administration, Post: after administration.

a): Number of dams showing abnormal signs at least once between Days 0 and 7 of lactation.

Table 5-1 General signs of female rats (recovery group) in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group	mg/kg	Number of females and general signs	Days of administration																									
			1		2		3		4		5		6		7		8		9		10		11		12		13	
			Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Control	0	Number of females	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	
		Normal	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	180	Number of females	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	
		Normal	6	6	6	6	6	6	6	6	6	6	6	3	6	5	6	6	6	6	6	4	6	3	6	4	6	2
		Salivation	0	0	0	0	0	0	0	0	0	0	0	3	0	1	0	0	0	0	0	2	0	3	0	2	0	4
	720	Number of females	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		Normal	6	6	6	3	6	4	6	5	6	3	6	0	6	2	6	0	6	0	6	0	5	1	5	0	5	0
		Salivation	0	0	0	2	0	2	0	0	0	3	0	6	0	4	0	6	0	6	0	6	0	5	0	5	0	5
		Soiled hair	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	1	1
		Decrease in locomotor activity	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
		Soiled perinasal area	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Perioral smudge	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1		
Death	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		

Pre: Before administration, Post: after administration.

Table 5-2 General signs of female rats (recovery group) in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group	mg/kg	Number of females and general signs	Days of administration																									
			14		15		16		17		18		19		20		21		22		23		24		25		26	
			Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Control	0	Number of females	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	
		Normal	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	180	Number of females	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	
		Normal	6	3	6	3	6	5	6	4	6	4	6	4	6	2	6	2	6	4	6	4	6	4	6	1	6	4
		Salivation	0	3	0	3	0	1	0	2	0	2	0	2	0	4	0	4	0	2	0	2	0	2	0	5	0	2
	720	Number of females	6	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
		Normal	5	0	5	0	5	1	5	0	5	0	5	0	5	0	5	0	5	0	5	0	5	0	5	0	5	0
		Salivation	0	5	0	5	0	4	0	5	0	5	0	5	0	5	0	5	0	5	0	5	0	5	0	5	0	5
		Soiled hair	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Decrease in locomotor activity	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Soiled perinasal area	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Perioral smudge		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Death	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		

Pre: Before administration, Post: after administration.

Table 5-3 General signs of female rats (recovery group) in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group	mg/kg	Number of females and general signs	Days of administration																									
			27		28		29		30		31		32		33		34		35		36		37		38		39	
			Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Control	0	Number of females	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	
		Normal	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	180	Number of females	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	
		Normal	6	4	6	4	6	2	6	1	6	2	6	3	6	3	6	1	6	3	6	6	6	6	6	6	6	6
	Salivation	0	2	0	2	0	4	0	5	0	4	0	3	0	3	0	5	0	3	0	0	0	0	0	0	0	0	
	720	Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	
		Normal	5	0	5	0	5	0	5	0	5	0	5	0	5	0	5	0	5	0	5	0	5	0	5	0	5	0
		Salivation	0	5	0	5	0	5	0	5	0	5	0	5	0	5	0	5	0	5	0	5	0	5	0	5	0	5
		Soiled hair	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Decrease in locomotor activity	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Soiled perinasal area	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		Perioral smudge	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Death		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	

Pre: Before administration, Post: after administration.

Table 5-4 General signs of female rats (recovery group) in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group	mg/kg	Number of females and general signs	Days of administration						Total ^{a)}
			40		41		42		
			Pre	Post	Pre	Post	Pre	Post	
Control	0	Number of females	6	6	6	6	6	6	6
		Normal	6	6	6	6	6	6	-
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	180	Number of females	6	6	6	6	6	6	6
		Normal	6	5	6	3	6	6	-
		Salivation	0	1	0	3	0	0	5
	720	Number of females	5	5	5	5	5	5	6
		Normal	5	0	5	0	5	0	-
		Salivation	0	5	0	5	0	5	6
		Soiled hair	0	0	0	0	0	0	2
		Decrease in locomotor activity	0	0	0	0	0	0	1
		Soiled perinasal area	0	0	0	0	0	0	1
		Perioral smudge	0	0	0	0	0	0	1
Death	0	0	0	0	0	0	1		

Pre: Before administration, Post: after administration.

a): Number of females showing abnormal signs at least once between Days 1 and 42 of administration.

Table 5-5 General signs of female rats (recovery group) in combined repeat dose and reproductive/developmental toxicity screening test of
 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group	mg/kg	Number of females and general signs	Days of recovery														
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Control	0	Number of females	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		Normal	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
1,1'-(1,1-dimethyl-3- methylene-1,3- propanediyl) bisbenzene	180	Number of females	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		Normal	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	720	Number of females	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
		Normal	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

Table 6 Body weights of male rats in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group	Control		1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene					
	0		45		180		720	
mg/kg								
Number of males	12		12		12		12	
Days of administration								
1	396 ± 14		396 ± 14		395 ± 14		396 ± 14	
4	407 ± 14		404 ± 15		398 ± 14		388 ± 12 **	
8	422 ± 13		422 ± 18		416 ± 16		401 ± 13 **	
11	435 ± 16		434 ± 20		429 ± 19		412 ± 15 **	
15	447 ± 16		448 ± 21		442 ± 21		422 ± 18 **	
18	454 ± 18		456 ± 25		449 ± 22		426 ± 20 **	
22	463 ± 21		468 ± 27		457 ± 23		435 ± 22 *	
25	473 ± 22		477 ± 27		466 ± 24		444 ± 22 *	
29	485 ± 23		487 ± 29		474 ± 24		449 ± 25 **	
32	493 ± 25		499 ± 30		483 ± 24		455 ± 30 **	
36	506 ± 26		508 ± 31		492 ± 22		465 ± 30 **	
39	510 ± 27		513 ± 32		499 ± 23		471 ± 30 **	
42	516 ± 26		523 ± 35		505 ± 24		477 ± 35 **	
Number of males	6		6		6		6	
Days of recovery								
1	515 ± 15		524 ± 28		513 ± 23		475 ± 44	
4	521 ± 15		530 ± 26		519 ± 25		476 ± 44 *	
8	532 ± 14		541 ± 29		531 ± 29		493 ± 47	
11	533 ± 14		544 ± 26		537 ± 29		496 ± 45	
14	541 ± 15		550 ± 26		547 ± 32		511 ± 44	

Each value shows mean (g) ± S.D.

Significantly different from control group (*: P<0.05, **: P<0.01).

Table 7 Body weights of female rats in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group	Control		1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene			
mg/kg	0		45	180		720
Number of females	12		12	12		12
Days of administration						
1	232 ± 8		231 ± 8	232 ± 8		232 ± 8
4	235 ± 8		234 ± 9	234 ± 10		225 ± 12 *
8	243 ± 7		240 ± 10	241 ± 9		232 ± 23
11	248 ± 8		248 ± 11	246 ± 11		246 ± 7 (11)
15	259 ± 7		255 ± 12	254 ± 12		252 ± 8 (11)
18	267 ± 13 (3)		260 ± 14 (4)	250 ± 13 (3)		260 ± 9 (3)
22	-		-	275 (2)		-
25	-		-	287 (2)		-

Each value shows mean (g) ± S.D.

Significantly different from control group (*: P<0.05).

Figures in parentheses indicate number of females.

Table 8 Body weights of dams during pregnancy in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group	Control	1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene			
mg/kg	0	45	180	720	
Number of dams	11	12	11	10	
Days of pregnancy					
0	265 ± 11	258 ± 13	261 ± 17	249 ± 10 *	
7	294 ± 14	288 ± 15	285 ± 20	278 ± 9	
14	326 ± 17	320 ± 17	314 ± 18	306 ± 12 *	
21	417 ± 27	412 ± 16 (11)	409 ± 31	362 ± 30 **	

Each value shows mean (g) ± S.D.

Significantly different from control group (*: P<0.05, **: P<0.01).

Figures in parentheses indicate number of dams.

Table 9 Body weights of dams during lactation in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group	Control	1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene		
	0	45	180	720
mg/kg				
Number of dams	11	12	11	10
Days of lactation				
0	306 ± 20	304 ± 15	298 ± 16	291 ± 13
4	314 ± 19	317 ± 15	300 ± 19	300 ± 15 (9)
6	297 ± 23	301 ± 18	297 ± 15 (10)	294 ± 15 (9)

Each value shows mean (g) ± S.D.

Figures in parentheses indicate number of dams.

Table 10 Body weights of female rats (recovery group) in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group		Control		1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene			
mg/kg		0		180		720	
Number of females		6		6		6	
Days of administration							
	1	236 ± 7		235 ± 8		236 ± 6	
	4	241 ± 7		240 ± 7		240 ± 7	
	8	247 ± 7		245 ± 7		249 ± 9	
	11	253 ± 10		252 ± 8		244 ± 29	
	15	258 ± 12		260 ± 8		259 ± 5	(5)
	18	265 ± 9		260 ± 12		267 ± 6	(5)
	22	273 ± 8		266 ± 8		271 ± 8	(5)
	25	277 ± 8		269 ± 6		276 ± 10	(5)
	29	282 ± 9		272 ± 7		277 ± 6	(5)
	32	284 ± 12		273 ± 5		279 ± 6	(5)
	36	288 ± 11		274 ± 3 *		283 ± 10	(5)
	39	289 ± 15		275 ± 5		284 ± 9	(5)
	42	292 ± 15		277 ± 5		290 ± 12	(5)
Number of females		6		6		5	
Days of recovery							
	1	291 ± 16		275 ± 4		291 ± 11	
	4	295 ± 14		280 ± 4 *		286 ± 13	
	8	300 ± 13		286 ± 6		288 ± 17	
	11	300 ± 13		287 ± 12		288 ± 18	
	14	307 ± 15		291 ± 15		294 ± 15	

Each value shows mean (g) ± S.D.

Figures in parentheses indicate number of females.

Significantly different from control group (*: P<0.05).

Table 11 Food consumption of male rats in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group	Control	1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene			
mg/kg	0	45	180	720	
Number of males	12	12	12	12	
Days of administration					
2	23 ± 3	24 ± 5	23 ± 4	22 ± 5	
5	25 ± 2	24 ± 4	24 ± 4	23 ± 3	
9	26 ± 3	25 ± 3	25 ± 4	23 ± 2	
12	25 ± 2	25 ± 4	24 ± 3	25 ± 2	
30	23 ± 3	22 ± 3	21 ± 2	25 ± 3	
33	22 ± 4	22 ± 3	23 ± 2	26 ± 3 **	
37	24 ± 4	24 ± 3	23 ± 2	29 ± 4 **	
40	20 ± 2	20 ± 3	19 ± 2	25 ± 5 **	
Number of males	6	6	6	6	
Days of recovery					
2	24 ± 2	24 ± 2	26 ± 3	30 ± 5 *	
5	28 ± 2	28 ± 3	29 ± 3	32 ± 4	
9	28 ± 3	29 ± 3	31 ± 2	32 ± 4	
12	28 ± 1	27 ± 2	30 ± 3	33 ± 4 *	

Each value shows mean (g/day) ± S.D.

Significantly different from control group (*: P<0.05, **: P<0.01).

Table 12 Food consumption of female rats in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group	Control	1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene		
mg/kg	0	45	180	720
Number of females	12	12	12	12
Days of administration				
2	13 ± 3	13 ± 2	13 ± 2	14 ± 4
5	16 ± 2	16 ± 3	16 ± 3	14 ± 4
9	14 ± 3	13 ± 2	13 ± 2	13 ± 3 (11)
12	18 ± 2	16 ± 2	16 ± 3	16 ± 3 (11)

Each value shows mean (g/day) ± S.D.

Figures in parentheses indicate number of females.

Table 13 Food consumption of dams during pregnancy in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group	Control	1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene		
mg/kg	0	45	180	720
Number of dams	11	12	11	10
Days of pregnancy				
2	17 ± 3	17 ± 3	16 ± 3	20 ± 3 *
9	19 ± 3	17 ± 3	18 ± 3	21 ± 2
16	21 ± 4	21 ± 2	21 ± 3	21 ± 2
20	21 ± 5	21 ± 3	22 ± 5	24 ± 3

Each value shows mean (g/day) ± S.D.

Significantly different from control group (*: P<0.05).

Table 14 Food consumption of dams during lactation in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group	Control	1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene		
mg/kg	0	45	180	720
Number of dams	11	12	11	9
Days of lactation	2	21 ± 7	23 ± 5	22 ± 3
		22 ± 7		

Each value shows mean (g/day) ± S.D.

Table 15 Food consumption of female rats (recovery group) in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group	Control	1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	
mg/kg	0	180	720
Number of females	6	6	6
Days of administration			
2	15 ± 2	15 ± 3	15 ± 3
5	16 ± 2	14 ± 2	14 ± 3
9	15 ± 1	12 ± 2 *	17 ± 2
12	16 ± 2	17 ± 2	14 ± 6
16	14 ± 2	15 ± 2	16 ± 2 (5)
19	13 ± 2	14 ± 2	17 ± 1 * (5)
23	13 ± 2	12 ± 3	18 ± 1 ** (5)
26	17 ± 2	18 ± 2	21 ± 2 * (5)
30	15 ± 2	16 ± 3	19 ± 4 (5)
33	14 ± 2	17 ± 3	17 ± 2 (5)
37	15 ± 1	19 ± 9	19 ± 3 (5)
40	14 ± 2	18 ± 5	18 ± 2 (5)
Number of females	6	6	5
Days of recovery			
2	16 ± 1	18 ± 4	20 ± 3
5	18 ± 2	20 ± 6	20 ± 3
9	21 ± 4	19 ± 5	21 ± 3
12	20 ± 3	19 ± 2	21 ± 3

Each value shows mean (g/day) ± S.D.

Significantly different from control group (*: P<0.05, **: P<0.01).

Figures in parentheses indicate number of females.

Table 16-1 FOB of male rats in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group		Control	1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene			
mg/kg		0	45	180	720	
Number of males		12	12	12	12	
Observation of animals in cages						
Posture	Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)	
	Mean (range)					
Mean (range)	Day 7	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)	
	Day 14	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)	
	Day 21	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)	
	Day 28	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)	
	Day 35	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)	
	Day 41	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)	
	Day 41	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)	
Palpebral closure	Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Mean (range)					
Mean (range)	Day 7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Day 14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Day 21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Day 28	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Day 35	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Day 41	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Day 41	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
Biting behavior	Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Mean (range)					
Mean (range)	Day 7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Day 14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Day 21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Day 28	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Day 35	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Day 41	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Day 41	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
Clonic convulsions	Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Mean (range)					
Mean (range)	Day 7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Day 14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Day 21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Day 28	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Day 35	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Day 41	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
	Day 41	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	

Findings were graded as follows

- Posture 1: Prone or recumbent position, 2: resting normally, 3: moving or running about, 4: jumping.
Palpebral closure 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.
Biting behavior 1: Not observed, 2: observed.
Clonic convulsions 1: Not observed, 2: jaw convulsions, 3: tremor.

Table 16-2 FOB of male rats in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group	Control	1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene			
mg/kg	0	45	180	720	
Number of males	12	12	12	12	
Observation of animals in cages					
Tonic convulsions	Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Mean (range)	Day 7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
	Day 14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
	Day 21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
	Day 28	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
	Day 35	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
	Day 41	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Findings were graded as follows

Tonic convulsions 1: Not observed, 2: tonic extension, 3: opisthotonus convulsions, 4: saltatory convulsions, 5: asphyxial convulsions.

Table 16-3 FOB of male rats in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group		1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene			
mg/kg		0	45	180	720
Number of males		12	12	12	12
Observation of animals on observer's palm					
Ease of removal from cage Mean (range)	Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
	Day 7	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
	Day 14	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
	Day 21	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
	Day 28	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
	Day 35	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
	Day 41	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
	Ease of handling Mean (range)	Pre	2.0 (2)	2.0 (2)	2.0 (2)
Day 7		2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 14		2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 21		2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 28		2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 35		2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 41		2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Muscle tone Mean (range)		Pre	2.0 (2)	2.0 (2)	2.0 (2)
	Day 7	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
	Day 14	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
	Day 21	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
	Day 28	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
	Day 35	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
	Day 41	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
	Fur conditions Mean (range)	Pre	1.0 (1)	1.0 (1)	1.0 (1)
Day 7		1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 14		1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 21		1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 28		1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 35		1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 41		1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Findings were graded as follows

- Ease of removal from cage 1: Docile and allowing itself to be handled, 2: rearing or cowering, 3: running about; hard to catch.
- Ease of handling 1: Docile and allowing itself to be handled, 2: struggling slightly or vocalizing, 3: struggling and trying to bite observer's hand.
- Muscle tone 1: Decreased, 2: normal, 3: increased.
- Fur conditions 1: Normal, 2: slightly soiled, 3: markedly soiled.

Table 16-4 FOB of male rats in combined repeat dose and reproductive/developmental toxicity screening test of 1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene by oral administration

Group		Control	1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene				
mg/kg		0	45	180	720		
Number of males		12	12	12	12		
Observation of animals on observer's palm							
Lacrimation	Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)		
	Mean (range)						
Mean (range)	Day 7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)		
	Day 14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)		
	Day 21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)		
	Day 28	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)		
	Day 35	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)		
	Day 41	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)		
	Salivation	Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	
		Mean (range)					
Day 7		1.0 (1)	1.0 (1)	1.3 (1-2)	1.7 (1-2) **		
Day 14		1.0 (1)	1.0 (1)	1.3 (1-2)	2.1 (1-3) **		
Day 21		1.0 (1)	1.0 (1)	1.3 (1-2) *	1.8 (1-2) **		
Day 28		1.0 (1)	1.0 (1)	1.2 (1-2)	1.8 (1-2) **		
Day 35		1.0 (1)	1.0 (1)	1.2 (1-2)	2.0 (2) **		
Day 41		1.0 (1)	1.0 (1)	1.3 (1-2) *	1.9 (1-2) **		
Respiration	Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)		
	Mean (range)						
	Day 7	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)		
	Day 14	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)		
	Day 21	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)		
	Day 28	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)		
	Day 35	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)		
	Day 41	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)		

Significantly different from control group (*: P<0.05, **: P<0.01).

Findings were graded as follows

Lacrimation 1: None, 2: mild, 3: marked.

Salivation 1: None, 2: mild, 3: marked.

Respiration 1: Normal, 2: bradypnea, 3: dyspnea.