

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

Pre: Before administration, Post: after administration.

Table 1-2 General signs 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	mg/kg	Number of males 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
Control	0	Number of males 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	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
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	45	Number of males 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	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 males Normal Salivation	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	4	12	6	12	8	12	9	12	5	12	8	12	9	12	8	12	9	12	9	12	9	12	8	12	9	12
	720	Number of males Normal Salivation Soiled hair	0	8	0	6	0	4	0	6	0	4	0	3	0	7	0	4	0	3	0	3	0	4	0	3	0	3	0
			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	1	12	0	12	0	12	1	12	0	12	1	12	3	12	0	12	0	12	0	12	2	12	2	12	2	12
			0	11	0	12	0	12	0	11	0	12	0	12	0	11	0	9	0	12	0	12	0	10	0	10	0	10	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	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	0	0	0

Pre: Before administration, Post: after administration.

Table 1-3 General signs 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	mg/kg	Number of males and general signs	Days of administration																																											
			27	28	29	30	31	32	33	34	35	36	37	38	39																															
Control	0	Number of males Normal	Pre	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	12	12	12	12	12	12	12								
			Post	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	12	12	12	12	12	12	12	12	12	12					
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	45	Number of males Normal	Pre	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	12	12	12	12	12	12	12	12	12	12					
			Post	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	12	12	12	12	12	12	12	12	12	12	12	12			
	180	Number of males Normal Salivation	Pre	12	7	12	8	12	9	12	9	12	5	12	4	12	7	12	7	12	9	12	9	12	9	12	9	12	9	12	7	12	7	12	9	12	9	12	10	12	7					
			Post	0	5	0	4	0	3	0	3	0	3	0	7	0	8	0	5	0	5	0	3	0	3	0	3	0	3	0	3	0	5	0	3	0	3	0	3	0	2	0	2	0	5	
	720	Number of males Normal Salivation Soiled hair	Pre	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	12	12	12	12	12	12	12	12	12	12	12	12	12		
			Post	12	0	12	0	12	0	12	0	12	0	12	0	12	0	12	0	12	0	12	0	12	0	12	0	12	0	12	0	12	0	12	0	12	0	12	0	12	0	12	0	12	0	12
Pre: Before administration, Post: after administration.			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	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Table 1-4 General signs 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	mg/kg	Number of males and general signs	Days of administration												Total <sup>a)</sup>
			40			41			42			43			
			Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post			
Control	0	Number of males Normal	12	12	12	12	12	12	6	12					12
			12	12	12	12	12	12	12	6					-
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	45	Number of males Normal	12	12	12	12	12	12	6	12					12
			12	12	12	12	12	12	6					-	
	180	Number of males Normal Salivation	12	12	12	12	12	6	12					12	
			12	11	12	2	12	5	6					-	
720	Number of males Normal Salivation Soiled hair	0	1	0	10	0	7	0	12					12	
		12	12	12	12	12	12	6	12					12	
		12	4	12	0	12	0	6						-	
		Salivation	0	8	0	12	0	12	0	12	0	12	0	12	
		Soiled hair	0	0	0	0	0	0	0	0	0	0	0	1	

Pre: Before administration, Post: after administration.

a) Number of males showing abnormal signs at least once between Days 1 and 43 of administration.

Table 1-5 General signs 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	mg/kg	Number of males 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 males	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	45	Number of males	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
	180	Number of males	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 males	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

Table 2-1 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																				
			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			
Control	0	Number of females	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	12	12	12	12	12	12	12	12	12	12	12	
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	45	Number of females	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	12	12	12	12	12	12	12	12	12	12	12	
	180	Number of females	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	12	12	12	12	12	12	12	12	12	12	12	
	Normal	Salivation	12	12	12	12	12	12	12	10	12	12	12	9	12	12	9	12	9	12	8	12	
			0	0	0	0	0	0	2	0	0	0	2	0	3	0	0	3	0	3	0	4	0
	720	Number of females	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
			12	12	12	12	5	11	7	9	8	10	6	10	3	9	2	10	5	10	6	11	4
	Normal	Salivation	0	0	0	1	0	7	0	5	0	3	0	6	0	9	0	6	0	5	0	7	0
			0	0	0	0	0	1	1	3	2	2	2	2	3	3	1	1	1	1	1	0	0
	Hypothermia	Decrease in locomotor activity	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	0	0	0	0	0	0
			0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	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	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Pre: Before administration, Post: after administration.

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 <sup>a)</sup>												
			15			16			17			18			19			20			21			22			23				24			25			26			27		
			Pre	Post	0	Pre	Post	0	Pre	Post	0	Pre	Post	0	Pre	Post	0	Pre	Post	0	Pre	Post	0	Pre	Post	0	Pre	Post	0		Pre	Post	0	Pre	Post	0						
Control	0	Number of females Normal	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	0	0	0	0	0	0	0	12							
			12	12	10	10	8	8	3	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-						
			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	0	0	0	0	0	0	0	12							
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	45	Number of females Normal	12	12	8	8	5	5	4	4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-							
			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	2	2	2	2	2	2	2	12							
			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	1	2	1	2	1	2	0	-	-						
720	Number of females Normal Salivation Soiled hair Hypothermia Decrease in locomotor activity Death	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	1	0	1	0	2	12										
		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	0	0	0	0	0	0	12								
		11	0	7	0	5	0	3	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-							

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			
Control	0	Number of dams	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
			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	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
			12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	180	Number of dams	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
			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	720	Number of dams	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
			11	3	11	8	11	6	11	6	11	6	11	6	11	6	11	6	11	6
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	720	Number of dams	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
			0	8	0	3	0	5	0	5	0	4	0	5	0	4	0	5	0	4
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	720	Number of dams	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
			10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	720	Number of dams	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
			9	1	10	2	10	0	10	0	10	0	10	0	10	0	10	0	10	0
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	720	Number of dams	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
			0	9	0	8	0	10	0	10	0	10	0	10	0	10	0	10	0	10
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	720	Number of dams	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
			1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	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 <sup>a)</sup>
			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	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		
		Normal	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		
		Normal	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		
		Normal	11	10	11	10	11	10	11	8	11	8	11	9	11	9	11	9	11	9	11	9	11	9	-		
	720	Salivation	0	1	0	1	0	1	0	3	0	3	0	2	0	2	0	2	0	2	0	2	0	2	9		
		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		
		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	10	0	9	0	8	0	5	-	-	-	-	10		
		Soiled hair	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1		
		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		

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 <sup>a)</sup>		
			0		1		2		3		4		5		6			7	
			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
			Normal	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
			Normal	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	11
			Normal	11	10	11	8	11	10	11	8	11	7	10	9	10	10	10	10
	720	Number of dams	0	1	0	3	0	1	0	3	0	3	0	3	0	1	0	0	4
			Salivation	10	10	10	9	9	9	9	9	9	9	9	9	9	9	9	9
		Number of dams	10	0	10	0	9	1	9	0	9	2	9	2	9	2	9	0	9
			Salivation	0	10	0	9	0	8	0	9	0	7	0	7	0	7	0	9

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	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	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	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	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	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	6	6	6	6	6	6	6	6	6	6	6	6	6	6			
			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	0	0	0	0	0	0	0	0		
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	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	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6			
		0	0	0	2	0	2	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
Normal	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	0	0	0	0	0	0	0	0				
	0	0	0	1	0	0	0	0	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	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	0	0	0	0	0	0	0				
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	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	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	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	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	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	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	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	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	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	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	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	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	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	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	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	4	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	4	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	
		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, Pos: 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		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 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	
		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	3	0	0	0	0	0	0
	720	Number of females Normal	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	
		Salivation	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
		Soiled hair	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
		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 smudgc	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 <sup>a)</sup>
			40		41		42		
			Pre	Post	Pre	Post	Pre	Post	
Control	0	Number of females Normal	6	6	6	6	6	6	6
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	180	Number of females Normal Salivation	6	6	6	6	6	6	6
	720	Number of females Normal Salivation Soiled hair Decrease in locomotor activity Soiled perinasal area Perioral smudge Death	5	5	5	5	5	5	6

Pre: Before administration, Post: after administration.  
a): Number of females showing abnormal signs at least once between Days 1 and 42 of administration.

Table S-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
1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	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 mg/kg	Control		1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	
	0	45	180	720
Number of males		12	12	12
Days of administration		12	12	12
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		6	6	6
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 mg/kg	Control		1,1-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	
	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	
mg/kg	0	45	180
Number of dams	11	12	11
Days of lactation			
0	306 ± 20	304 ± 15	298 ± 16
4	314 ± 19	317 ± 15	300 ± 19
6	297 ± 23	301 ± 18	297 ± 15 (10)
			291 ± 13
			300 ± 15 (9)
			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	
	0	180	720	
mg/kg				
Number of females	6	6	6	6
Days of administration				
1	236 ± 7	235 ± 8	236 ± 6	6
4	241 ± 7	240 ± 7	240 ± 7	7
8	247 ± 7	245 ± 7	249 ± 9	9
11	253 ± 10	252 ± 8	244 ± 29	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	11
4	295 ± 14	280 ± 4*	286 ± 13	13
8	300 ± 13	286 ± 6	288 ± 17	17
11	300 ± 13	287 ± 12	288 ± 18	18
14	307 ± 15	291 ± 15	294 ± 15	15

Each value shows mean (±) 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-propanediyl)bisbenzene by oral administration

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

Group	Control	1,1'-(1,1-dimethyl-3-propanediyl)bisbenzene	
mg/kg	0	45	180
Number of dams	11	12	11
Days of lactation	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	180	720
mg/kg	0			
Number of females	6	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	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 mg/kg	Control		1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	
	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)
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)
Palpebral closure				
Pre	1.0 (1)	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)
Biting behavior				
Pre	1.0 (1)	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)
Clonic convulsions				
Pre	1.0 (1)	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

- 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	180	720
mg/kg	0	45	180	720
Number of males	12	12	12	12
Observation of animals in cages				
Tonic convulsions	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Mean (range)	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Pre	1.0 (1)	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

Tonic convulsions 1: Not observed, 2: tonic extension, 3: opisthotonus convulsions, 4: salatory 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	Control		1,1-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	
	0	12	180	720
mg/kg				
Number of males				
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)	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)	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)	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 mg/kg	Control		1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	
	0	45	180	720
Number of males	12	12	12	12
Observation of animals on observer's palm				
Lacrimation	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Mean (range)	1.0 (1)	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)
Salivation	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Mean (range)	1.0 (1)	1.0 (1)	1.3 (1-2)	1.7 (1-2) **
Day 7	1.0 (1)	1.0 (1)	1.3 (1-2)	2.1 (1-3) **
Day 14	1.0 (1)	1.0 (1)	1.3 (1-2)	1.8 (1-2) **
Day 21	1.0 (1)	1.0 (1)	1.2 (1-2)	1.8 (1-2) **
Day 28	1.0 (1)	1.0 (1)	1.2 (1-2)	2.0 (2) **
Day 35	1.0 (1)	1.0 (1)	1.3 (1-2)	1.9 (1-2) **
Day 41	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Respiration	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Mean (range)	1.0 (1)	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)

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.

Table 16-5 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 mg/kg	Control		1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	
	0	45	180	720
Number of males	12	12	12	12
Open-field test				
Frequency of rearing Mean ± S.D.	Pre 5.2 ± 3.7	2.8	4.5 ± 4.7	4.6 ± 3.1
	Day 7 11.4 ± 4.1	5.2	9.3 ± 4.5	6.7 ± 4.2*
	Day 14 3.6 ± 2.4	2.4	3.3 ± 3.3	4.3 ± 3.9
	Day 21 2.7 ± 2.9	2.7	2.5 ± 2.2	2.8 ± 4.2
	Day 28 4.8 ± 2.2	3.9	2.8 ± 2.6	3.0 ± 2.9
	Day 35 7.3 ± 4.0	3.4	7.2 ± 3.1	4.6 ± 3.3
	Day 41 4.9 ± 2.5	4.4	3.1 ± 2.8	4.5 ± 3.1
Frequency of grooming Mean ± S.D.	Pre 0.0 ± 0.0	0.0	0.0 ± 0.0	0.0 ± 0.0
	Day 7 0.0 ± 0.0	0.0	0.0 ± 0.0	0.0 ± 0.0
	Day 14 0.0 ± 0.0	0.0	0.0 ± 0.0	0.0 ± 0.0
	Day 21 0.2 ± 0.6	0.0	0.0 ± 0.0	0.0 ± 0.0
	Day 28 0.0 ± 0.0	0.0	0.0 ± 0.0	0.0 ± 0.0
	Day 35 0.0 ± 0.0	0.0	0.0 ± 0.0	0.0 ± 0.0
	Day 41 0.0 ± 0.0	0.0	0.0 ± 0.0	0.0 ± 0.0
Gait Mean (range)	Pre 1.0 (1)	(1)	1.0 (1)	1.0 (1)
	Day 7 1.0 (1)	(1)	1.0 (1)	1.0 (1)
	Day 14 1.0 (1)	(1)	1.0 (1)	1.0 (1)
	Day 21 1.0 (1)	(1)	1.0 (1)	1.0 (1)
	Day 28 1.0 (1)	(1)	1.0 (1)	1.0 (1)
	Day 35 1.0 (1)	(1)	1.0 (1)	1.0 (1)
	Day 41 1.0 (1)	(1)	1.0 (1)	1.0 (1)
Palpebral closure Mean (range)	Pre 1.0 (1)	(1)	1.0 (1)	1.0 (1)
	Day 7 1.0 (1)	(1)	1.0 (1)	1.0 (1)
	Day 14 1.0 (1)	(1)	1.0 (1)	1.0 (1)
	Day 21 1.0 (1)	(1)	1.0 (1)	1.0 (1)
	Day 28 1.0 (1)	(1)	1.0 (1)	1.0 (1)
	Day 35 1.0 (1)	(1)	1.0 (1)	1.0 (1)
	Day 41 1.0 (1)	(1)	1.0 (1)	1.0 (1)

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

Frequency of rearing (during a 2-minute period).

Frequency of grooming (during a 2-minute period).

Findings were graded as follows

Gait

- 1: Normal, 2: unmoving, 3: staggering, 4: hind-limbs extended and dragged, 5: all fours extended, 6: forelimbs extended and dragged; unable to support body, 7: standing on tiptoes.

Palpebral closure

- 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

Table 16-6 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	
	0	45	180	720
mg/kg				
Number of males	12	12	12	12
Open-field test				
Consciousness				
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)
Behavioral abnormalities				
Mean (range)				
Pre	1.0 (1)	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)
Righting reflex				
Mean (range)				
Pre	1.0 (1)	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

Consciousness 1: Comatose; no response, 2: exploring behavior, 3: excited and moving spasmodically.

Behavioral abnormalities 1: Not observed, 2: straub's reaction, 3: moving backward, 4: writhing.

Righting reflex 1: Righting itself immediately, 2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

Table 17-1 FOB 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	Control		1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	
	0	45	180	720
Number of females	12	12	12	12
Observation of animals in cages				
Posture				
Mean (range)				
Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 8	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 15	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 1 of pregnancy	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 8 of pregnancy	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 15 of pregnancy	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 3 of lactation	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Palpebral closure				
Mean (range)				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 1 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 3 of lactation	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Biting behavior				
Mean (range)				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 1 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 3 of lactation	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Clonic convulsions				
Mean (range)				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 1 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 3 of lactation	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Figures in parentheses [ ] indicate number of females.

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 17-2 FOB 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	Control		1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	
	0	45	180	720
Number of females	12	12	12	12
Observation of animals in cages				
Tonic convulsions	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Mean (range)	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 1 of pregnancy	[11]	[11]	[11]	[11]
Day 8 of pregnancy	[11]	[11]	[11]	[10]
Day 15 of pregnancy	[11]	[11]	[11]	[10]
Day 3 of lactation	[11]	[11]	[11]	[10]
Figures in parentheses [ ] indicate number of females.				
Findings were graded as follows				
Tonic convulsions				

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

Table 17-3 FOB 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	
	0	45	130	720
Number of females	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 8	2.0 (2)	2.0 (2)	2.0 (2)	1.9 (1-2)
Day 15	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 1 of pregnancy	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 8 of pregnancy	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 15 of pregnancy	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 3 of lactation	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)	2.0 (2)
Day 8	2.0 (2)	2.0 (2)	2.0 (2)	1.9 (1-2)
Day 15	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 1 of pregnancy	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 8 of pregnancy	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 15 of pregnancy	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 3 of lactation	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)	2.0 (2)
Day 8	2.0 (2)	2.0 (2)	2.0 (2)	1.9 (1-2)
Day 15	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 1 of pregnancy	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 8 of pregnancy	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 15 of pregnancy	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 3 of lactation	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)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	1.3 (1-3)*
Day 15	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 1 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 3 of lactation	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Figures in parentheses [ ] indicate number of females.

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

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 17-4 FOB 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	Control		1,1-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	
	0	45	180	720
Number of females	12	12	12	12
Observation of animals on observers' palm				
Lacrimation				
Mean (range)				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 1 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 3 of lactation	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Salivation				
Mean (range)				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	1.7 (1-2) **
Day 15	1.0 (1)	1.0 (1)	1.2 (1-2)	1.9 (1-2) **
Day 1 of pregnancy	1.0 (1)	1.0 (1)	1.1 (1-2)	1.7 (1-3) **
Day 8 of pregnancy	1.0 (1)	1.0 (1)	1.3 (1-2)	1.7 (1-2) **
Day 15 of pregnancy	1.0 (1)	1.0 (1)	1.1 (1-2)	1.8 (1-2) **
Day 3 of lactation	1.0 (1)	1.0 (1)	1.2 (1-2)	2.0 (2) **
Respiration				
Mean (range)				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 1 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 3 of lactation	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Figures in parentheses [ ] indicate number of females.

Significantly different from control group (\*\*; 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.

Table 17-5 FOB 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	
	0	45	180	720
mg/kg				
Number of females	12	12	12	12
Open-field test				
Frequency of rearing				
Mean ± S.D.				
Pre	7.6 ± 4.6	8.8 ± 4.7	10.3 ± 6.0	7.6 ± 3.9
Day 8	9.3 ± 4.7	10.7 ± 4.0	9.2 ± 5.4	7.0 ± 3.2
Day 15	8.3 ± 4.1	10.4 ± 5.6	11.2 ± 5.4	7.6 ± 3.6
Day 1 of pregnancy	4.5 ± 3.9	6.8 ± 4.0	5.7 ± 2.4	5.7 ± 3.7
Day 8 of pregnancy	6.5 ± 3.4	9.0 ± 4.4	8.6 ± 3.0	5.7 ± 3.6
Day 15 of pregnancy	8.2 ± 4.3	10.3 ± 3.5	7.1 ± 3.4	7.3 ± 4.6
Day 3 of lactation	9.6 ± 6.4	11.0 ± 6.2	7.3 ± 4.0	7.6 ± 1.9
				[11]
Frequency of grooming				
Mean ± S.D.				
Pre	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Day 8	0.2 ± 0.6	0.1 ± 0.3	0.0 ± 0.0	0.2 ± 0.4
Day 15	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Day 1 of pregnancy	0.0 ± 0.0	0.0 ± 0.0	0.1 ± 0.3	0.1 ± 0.3
Day 8 of pregnancy	0.0 ± 0.0	0.1 ± 0.3	0.1 ± 0.3	0.0 ± 0.0
Day 15 of pregnancy	0.3 ± 0.9	0.1 ± 0.3	0.0 ± 0.0	0.0 ± 0.0
Day 3 of lactation	0.4 ± 0.7	0.0 ± 0.0*	0.0 ± 0.0*	0.0 ± 0.0
				[11]
Gait				
Mean (range)				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 1 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 3 of lactation	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
				[11]
Palpebral closure				
Mean (range)				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 1 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 3 of lactation	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
				[11]

Figures in parentheses ( ) indicate number of females.

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

Frequency of rearing (during a 2-minute period).

Frequency of grooming (during a 2-minute period).

Findings were graded as follows

Gait

1: Normal, 2: unmoving, 3: staggering, 4: hind-limbs extended and dragged, 5: all fours extended,

6: forelimbs extended and dragged; unable to support body, 7: standing on tiptoe.

Palpebral closure

1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

Table 17-6 FOB 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	Control		1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	
	0	45	180	720
Number of females	12	12	12	12
Open-field test				
Consciousness Mean (range)				
Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 8	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 15	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 1 of pregnancy	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 8 of pregnancy	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 15 of pregnancy	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 3 of lactation	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Behavioral abnormalities Mean (range)				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 1 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 3 of lactation	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Righting reflex Mean (range)				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 1 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15 of pregnancy	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 3 of lactation	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Figures in parentheses [ ] indicate number of females.

Findings were graded as follows

Consciousness

Behavioral abnormalities

Righting reflex

1: Comatose; no response, 2: exploring behavior, 3: excited and moving spasmodically.

1: Not observed, 2: straub's reaction, 3: moving backward, 4: writhing.

1: Righting itself immediately, 2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

Table 18-1 FOB 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	Control		1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	
	0	6	180	720
Number of females	6	6	6	6
Observation of animals in cages				
Posture				
Mean (range)	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 8	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 15	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 22	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 29	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 36	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 42	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Palpebral closure				
Mean (range)	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 22	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 29	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 36	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 42	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Biting behavior				
Mean (range)	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 22	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 29	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 36	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 42	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Clonic convulsions				
Mean (range)	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 22	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 29	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 36	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 42	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Figures in parentheses ( ) indicate number of females.

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 18-2 FOB 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
Number of females	6	6
Observation of animals in cages		
Tonic convulsions	1.0 (1)	1.0 (1)
Mean (range)	1.0 (1)	1.0 (1)
Pre	1.0 (1)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)
Day 15	1.0 (1)	1.0 (1)
Day 22	1.0 (1)	1.0 (1)
Day 29	1.0 (1)	1.0 (1)
Day 36	1.0 (1)	1.0 (1)
Day 42	1.0 (1)	1.0 (1)

Figures in parentheses [ ] indicate number of females.

Findings were graded as follows

Tonic convulsions

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

Table 18-3 FOB 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	
	0	6	180	720
Number of females	6	6	6	6
Observation of animals on observer's palm				
Ease of removal from cage				
Mean (range)	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 8	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 15	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 22	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 29	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 36	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 42	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Ease of handling				
Mean (range)	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 8	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 15	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 22	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 29	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 36	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 42	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Muscle tone				
Mean (range)	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 8	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 15	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 22	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 29	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 36	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Day 42	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Fur conditions				
Mean (range)	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 22	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 29	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 36	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 42	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Figures in parentheses [ ] indicate number of females.

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 18-4 FOB 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	Control		1,1-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	
	0	180	180	720
Number of females	6		6	
Observation of animals on observer's palm				
Lacrimation	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Mean (range)	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 22	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 29	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 36	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 42	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)
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	1.8 (1-2) **
Day 15	1.0 (1)	1.0 (1)	1.3 (1-2)	2.0 (2) **
Day 22	1.0 (1)	1.0 (1)	1.0 (1)	2.0 (2) **
Day 29	1.0 (1)	1.0 (1)	1.7 (1-2) **	2.0 (2) **
Day 36	1.0 (1)	1.0 (1)	1.0 (1)	1.8 (1-2) **
Day 42	1.0 (1)	1.0 (1)	1.0 (1)	2.0 (2) **
Respiration				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 15	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 22	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 29	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 36	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Day 42	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)

Figures in parentheses [ ] indicate number of females.

Significantly different from control group (\*\*: 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.

Table 18-5 FOB 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	
	0	180	720	6
mg/kg				
Number of females	6	6	6	6
Open-field test				
Frequency of rearing				
Mean ± S.D.				
Pre	4.7 ± 2.9	5.8 ± 4.3	6.5 ± 2.3	
Day 8	6.8 ± 4.4	6.0 ± 2.2	5.7 ± 1.5	
Day 15	8.0 ± 3.5	6.7 ± 3.0	10.4 ± 3.2	[5]
Day 22	3.8 ± 1.0	4.3 ± 1.6	3.0 ± 1.0	[5]
Day 29	7.8 ± 3.9	4.7 ± 1.8	9.4 ± 3.6	[5]
Day 36	8.3 ± 1.4	7.8 ± 3.7	7.6 ± 5.7	[5]
Day 42	4.8 ± 2.6	6.0 ± 3.8	7.0 ± 4.9	[5]
Frequency of grooming				
Mean ± S.D.				
Pre	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	
Day 8	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	
Day 15	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	[5]
Day 22	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	[5]
Day 29	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	[5]
Day 36	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	[5]
Day 42	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	[5]
Gait				
Mean (range)				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	
Day 15	1.0 (1)	1.0 (1)	1.0 (1)	[5]
Day 22	1.0 (1)	1.0 (1)	1.0 (1)	[5]
Day 29	1.0 (1)	1.0 (1)	1.0 (1)	[5]
Day 36	1.0 (1)	1.0 (1)	1.0 (1)	[5]
Day 42	1.0 (1)	1.0 (1)	1.0 (1)	[5]
Palpebral closure				
Mean (range)				
Pre	1.0 (1)	1.0 (1)	1.0 (1)	
Day 8	1.0 (1)	1.0 (1)	1.0 (1)	
Day 15	1.0 (1)	1.0 (1)	1.0 (1)	[5]
Day 22	1.0 (1)	1.0 (1)	1.0 (1)	[5]
Day 29	1.0 (1)	1.0 (1)	1.0 (1)	[5]
Day 36	1.0 (1)	1.0 (1)	1.0 (1)	[5]
Day 42	1.0 (1)	1.0 (1)	1.0 (1)	[5]

Figures in parentheses [ ] indicate number of females.

Frequency of rearing (during a 2-minute period).

Frequency of grooming (during a 2-minute period).

Findings were graded as follows

Gait

- 1: Normal, 2: unmovng, 3: staggering, 4: hind-limbs extended and dragged, 5: all fours extended, 6: forelimbs extended and dragged; unable to support body, 7: standing on tiptoe.

Palpebral closure.

- 1: Eyelids open normally, 2: eyelids half-closed, 3: eyelids closed.

Table 18-5 FOB 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	720
Number of females	6	6
<b>Open-field test</b>		
<b>Consciousness</b>		
Mean (range)		
Pre	2.0 (2)	2.0 (2)
Day 8	2.0 (2)	2.0 (2)
Day 15	2.0 (2)	2.0 (2)
Day 22	2.0 (2)	2.0 (2) [5]
Day 29	2.0 (2)	2.0 (2) [5]
Day 36	2.0 (2)	2.0 (2) [5]
Day 42	2.0 (2)	2.0 (2) [5]
<b>Behavioral abnormalities</b>		
Mean (range)		
Pre	1.0 (1)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)
Day 15	1.0 (1)	1.0 (1)
Day 22	1.0 (1)	1.0 (1) [5]
Day 29	1.0 (1)	1.0 (1) [5]
Day 36	1.0 (1)	1.0 (1) [5]
Day 42	1.0 (1)	1.0 (1) [5]
<b>Righting reflex</b>		
Mean (range)		
Pre	1.0 (1)	1.0 (1)
Day 8	1.0 (1)	1.0 (1)
Day 15	1.0 (1)	1.0 (1)
Day 22	1.0 (1)	1.0 (1) [5]
Day 29	1.0 (1)	1.0 (1) [5]
Day 36	1.0 (1)	1.0 (1) [5]
Day 42	1.0 (1)	1.0 (1) [5]

Figures in parentheses [ ] indicate number of females.

Findings were graded as follows

- Consciousness 1: Comatose; no response, 2: exploring behavior, 3: excited and moving spasmodically.
- Behavioral abnormalities 1: Not observed, 2: Straub's reaction, 3: moving backward, 4: writhing.
- Righting reflex 1: Righting itself immediately, 2: requiring 3 seconds or longer to right itself, 3: unable to right itself.

Table 19 Sensory response of male rats on termination of administration period 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	45	180	720
Number of males	6	6	6	6	6	6
Pupillary reflex						
Mean (range)	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Approaching behavior						
Mean (range)	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Response to touch						
Mean (range)	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Auditory reflex						
Mean (range)	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Pain reflex						
Mean (range)	3.0 (3)	3.0 (3)	3.0 (3)	3.0 (3)	3.0 (3)	3.0 (3)

Findings were graded as follows.

Pupillary reflex

Approaching behavior

Response to touch

Auditory reflex

Pain reflex

1: Normal pupillary contraction observed, 2: pupils completely dilated, 3: pupils completely contracted.

1: Not observed, 2: approaching and sniffing stimulus, 3: reacting to stimulus, including vocalizing,

4: jumping at or biting at stimulus.

1: No response, 2: looking back and leaving stimulus, 3: reacting to stimulus, including vocalizing,

4: jumping at or biting at stimulus.

1: Not observed, 2: hesitating at stimulus or moving ears, 3: jumping at and trying to bite at the source of sound.

1: Not observed, 2: slowly looking back or slowly moving forward to escape from stimulus,

3: quickly moving forward to escape from stimulus or biting at it immediately after looking back,

4: jumping forward to escape from stimulus, 5: loudly vocalizing and biting at stimulus after suddenly looking back.

Table 20 Sensory response of female rats on termination of administration period 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
Number of females	6	6	6	6
Pupillary reflex				
Mean (range)	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Approaching behavior				
Mean (range)	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Response to touch				
Mean (range)	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Auditory reflex				
Mean (range)	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Pain reflex				
Mean (range)	3.0 (3)	3.0 (3)	3.0 (3)	3.0 (3)

Findings were graded as follows.

Pupillary reflex 1: Normal pupillary contraction observed, 2: pupils completely dilated, 3: pupils completely contracted.

Approaching behavior 1: Not observed, 2: approaching and sniffing stimulus, 3: reacting to stimulus, including vocalizing,

4: jumping at or biting at stimulus.

Response to touch

1: No response, 2: looking back and leaving stimulus, 3: reacting to stimulus, including vocalizing,

4: jumping at or biting at stimulus.

Auditory reflex

1: Not observed, 2: hesitating at stimulus or moving ears, 3: jumping at and trying to bite at the source of sound.

Pain reflex

1: Not observed, 2: slowly moving forward to escape from stimulus,

3: quickly moving forward to escape from stimulus or biting at it immediately after looking back,

4: jumping forward to escape from stimulus, 5: loudly vocalizing and biting at stimulus after suddenly looking back.