

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		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			
Open-field test											
Frequency of rearing	Pre	5.2 ±	3.7	3.3 ±	2.8	4.5 ±	4.7	4.6 ±	3.1		
	Mean ± S.D.										
Mean ± S.D.	Day 7	11.4 ±	4.1	7.0 ±	5.2	9.3 ±	4.5	6.7 ±	4.2 *		
	Day 14	3.6 ±	2.4	3.1 ±	2.4	3.3 ±	3.3	4.3 ±	3.9		
	Day 21	2.7 ±	2.9	2.8 ±	2.7	2.5 ±	2.2	2.8 ±	4.2		
	Day 28	4.8 ±	2.2	3.9 ±	3.9	2.8 ±	2.6	3.0 ±	2.9		
	Day 35	7.3 ±	4.0	4.9 ±	3.4	7.2 ±	3.1	4.6 ±	3.3		
	Day 41	4.9 ±	2.5	5.0 ±	4.4	3.1 ±	2.8	4.5 ±	3.1		
	Day 41	4.9 ±	2.5	5.0 ±	4.4	3.1 ±	2.8	4.5 ±	3.1		
Frequency of grooming	Pre	0.0 ±	0.0	0.0 ±	0.0	0.0 ±	0.0	0.0 ±	0.0		
	Mean ± S.D.										
Mean ± S.D.	Day 7	0.0 ±	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 ±	0.0		
	Day 21	0.2 ±	0.6	0.0 ±	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 ±	0.0		
	Day 35	0.0 ±	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 ±	0.0		
	Day 41	0.0 ±	0.0	0.0 ±	0.0	0.0 ±	0.0	0.0 ±	0.0		
Gait	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)		
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)		

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 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			
mg/kg		0	45	180	720	
Number of males		12	12	12	12	
Open-field test						
Consciousness	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)	
Behavioral abnormalities	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)	
Righting reflex	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

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		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	
Observation of animals in cages									
Posture	Pre	2.0	(2)	2.0	(2)	2.0	(2)	2.0	(2)
	Mean (range)	2.0	(2)	2.0	(2)	2.0	(2)	2.0	(2)
Mean (range)	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)	[11]	2.0	(2)	[11]	2.0	(2)
	Day 8 of pregnancy	2.0	(2)	[11]	2.0	(2)	[11]	2.0	(2)
	Day 15 of pregnancy	2.0	(2)	[11]	2.0	(2)	[11]	2.0	(2)
	Day 3 of lactation	2.0	(2)	[11]	2.0	(2)	[11]	2.0	(2)
	Day 3 of lactation	2.0	(2)	[11]	2.0	(2)	[11]	2.0	(2)
Palpebral closure	Pre	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)
Mean (range)	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)	[11]	1.0	(1)	[11]	1.0	(1)
	Day 8 of pregnancy	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1)
	Day 15 of pregnancy	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1)
	Day 3 of lactation	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1)
	Day 3 of lactation	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1)
Biting behavior	Pre	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)
Mean (range)	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)	[11]	1.0	(1)	[11]	1.0	(1)
	Day 8 of pregnancy	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1)
	Day 15 of pregnancy	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1)
	Day 3 of lactation	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1)
	Day 3 of lactation	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1)
Clonic convulsions	Pre	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)
Mean (range)	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)	[11]	1.0	(1)	[11]	1.0	(1)
	Day 8 of pregnancy	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1)
	Day 15 of pregnancy	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1)
	Day 3 of lactation	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1)
	Day 3 of lactation	1.0	(1)	[11]	1.0	(1)	[11]	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		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		
Observation of animals in cages										
Tonic convulsions		Pre		1.0 (1)		1.0 (1)		1.0 (1)		1.0 (1)
Mean (range)		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) [11]
		Day 1 of pregnancy		1.0 (1) [11]		1.0 (1)		1.0 (1) [11]		1.0 (1) [10]
		Day 8 of pregnancy		1.0 (1) [11]		1.0 (1)		1.0 (1) [11]		1.0 (1) [10]
		Day 15 of pregnancy		1.0 (1) [11]		1.0 (1)		1.0 (1) [11]		1.0 (1) [10]
		Day 3 of lactation		1.0 (1) [11]		1.0 (1)		1.0 (1) [11]		1.0 (1) [9]

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 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		1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene			
mg/kg		0	45	180	720
Number of females		12	12	12	12
Observation of animals on observer's palm					
Ease of removal from cage	Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
	Mean (range)				
Ease of handling	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) [11]
	Day 1 of pregnancy	2.0 (2) [11]	2.0 (2)	2.0 (2) [11]	2.0 (2) [10]
	Day 8 of pregnancy	2.0 (2) [11]	2.0 (2)	2.0 (2) [11]	2.0 (2) [10]
	Day 15 of pregnancy	2.0 (2) [11]	2.0 (2)	2.0 (2) [11]	2.0 (2) [10]
	Day 3 of lactation	2.0 (2) [11]	2.0 (2)	2.0 (2) [11]	2.0 (2) [9]
	Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Muscle tone	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) [11]
	Day 1 of pregnancy	2.0 (2) [11]	2.0 (2)	2.0 (2) [11]	2.0 (2) [10]
	Day 8 of pregnancy	2.0 (2) [11]	2.0 (2)	2.0 (2) [11]	2.0 (2) [10]
	Day 15 of pregnancy	2.0 (2) [11]	2.0 (2)	2.0 (2) [11]	2.0 (2) [10]
	Day 3 of lactation	2.0 (2) [11]	2.0 (2)	2.0 (2) [11]	2.0 (2) [9]
	Pre	2.0 (2)	2.0 (2)	2.0 (2)	2.0 (2)
Fur conditions	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) [11]
	Day 1 of pregnancy	2.0 (2) [11]	2.0 (2)	2.0 (2) [11]	2.0 (2) [10]
	Day 8 of pregnancy	2.0 (2) [11]	2.0 (2)	2.0 (2) [11]	2.0 (2) [10]
	Day 15 of pregnancy	2.0 (2) [11]	2.0 (2)	2.0 (2) [11]	2.0 (2) [10]
	Day 3 of lactation	2.0 (2) [11]	2.0 (2)	2.0 (2) [11]	2.0 (2) [9]
	Pre	1.0 (1)	1.0 (1)	1.0 (1)	1.0 (1)
Fur conditions	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) [11]
	Day 1 of pregnancy	1.0 (1) [11]	1.0 (1)	1.0 (1) [11]	1.0 (1) [10]
	Day 8 of pregnancy	1.0 (1) [11]	1.0 (1)	1.0 (1) [11]	1.0 (1) [10]
	Day 15 of pregnancy	1.0 (1) [11]	1.0 (1)	1.0 (1) [11]	1.0 (1) [10]
	Day 3 of lactation	1.0 (1) [11]	1.0 (1)	1.0 (1) [11]	1.0 (1) [9]
	Pre	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		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	
Observation of animals on observer's palm									
Lacrimation	Pre	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)
Mean (range)	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) [11]
	Day 1 of pregnancy	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1) [10]
	Day 8 of pregnancy	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1) [10]
	Day 15 of pregnancy	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1) [10]
	Day 3 of lactation	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1) [9]
	Day 3 of lactation	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1) [9]
Salivation	Pre	1.0	(1)	1.0	(1)	1.0	(1)	1.0	(1)
	Mean (range)	1.0	(1)	1.0	(1)	1.0	(1)	1.7	(1-2) **
Mean (range)	Day 8	1.0	(1)	1.0	(1)	1.2	(1-2)	1.9	(1-2) ** [11]
	Day 15	1.0	(1)	1.0	(1)	1.1	(1-2)	1.7	(1-3) ** [10]
	Day 1 of pregnancy	1.0	(1)	[11]	1.0	(1)	[11]	1.3	(1-2) ** [10]
	Day 8 of pregnancy	1.0	(1)	[11]	1.0	(1)	[11]	1.8	(1-2) ** [10]
	Day 15 of pregnancy	1.0	(1)	[11]	1.0	(1)	[11]	2.0	(2) ** [9]
	Day 3 of lactation	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1)
	Day 3 of lactation	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1)
Respiration	Pre	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)
Mean (range)	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) [11]
	Day 1 of pregnancy	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1) [10]
	Day 8 of pregnancy	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1) [10]
	Day 15 of pregnancy	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1) [10]
	Day 3 of lactation	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1) [9]
	Day 3 of lactation	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1) [9]

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 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								
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	[11]		
	Day 1 of pregnancy	4.5 ± 3.9 [11]	6.8 ± 4.0	5.7 ± 2.4 [11]	5.7 ± 3.7 [10]			
	Day 8 of pregnancy	6.5 ± 3.4 [11]	9.0 ± 4.4	8.6 ± 3.0 [11]	5.7 ± 3.6 [10]			
	Day 15 of pregnancy	8.2 ± 4.3 [11]	10.3 ± 3.5	7.1 ± 3.4 [11]	7.3 ± 4.6 [10]			
	Day 3 of lactation	9.6 ± 6.4 [11]	11.0 ± 6.2	7.3 ± 4.0 [11]	7.6 ± 1.9 [9]			
	Day 3 of lactation	9.6 ± 6.4 [11]	11.0 ± 6.2	7.3 ± 4.0 [11]	7.6 ± 1.9 [9]			
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	[11]		
	Day 1 of pregnancy	0.0 ± 0.0 [11]	0.0 ± 0.0	0.1 ± 0.3 [11]	0.1 ± 0.3 [10]			
	Day 8 of pregnancy	0.0 ± 0.0 [11]	0.1 ± 0.3	0.1 ± 0.3 [11]	0.0 ± 0.0 [10]			
	Day 15 of pregnancy	0.3 ± 0.9 [11]	0.1 ± 0.3	0.0 ± 0.0 [11]	0.0 ± 0.0 [10]			
	Day 3 of lactation	0.4 ± 0.7 [11]	0.0 ± 0.0 *	0.0 ± 0.0 * [11]	0.0 ± 0.0 [9]			
	Day 3 of lactation	0.4 ± 0.7 [11]	0.0 ± 0.0 *	0.0 ± 0.0 * [11]	0.0 ± 0.0 [9]			
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)	[11]		
	Day 1 of pregnancy	1.0 (1) [11]	1.0 (1)	1.0 (1) [11]	1.0 (1) [10]			
	Day 8 of pregnancy	1.0 (1) [11]	1.0 (1)	1.0 (1) [11]	1.0 (1) [10]			
	Day 15 of pregnancy	1.0 (1) [11]	1.0 (1)	1.0 (1) [11]	1.0 (1) [10]			
	Day 3 of lactation	1.0 (1) [11]	1.0 (1)	1.0 (1) [11]	1.0 (1) [9]			
	Day 3 of lactation	1.0 (1) [11]	1.0 (1)	1.0 (1) [11]	1.0 (1) [9]			
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)	[11]		
	Day 1 of pregnancy	1.0 (1) [11]	1.0 (1)	1.0 (1) [11]	1.0 (1) [10]			
	Day 8 of pregnancy	1.0 (1) [11]	1.0 (1)	1.0 (1) [11]	1.0 (1) [10]			
	Day 15 of pregnancy	1.0 (1) [11]	1.0 (1)	1.0 (1) [11]	1.0 (1) [10]			
	Day 3 of lactation	1.0 (1) [11]	1.0 (1)	1.0 (1) [11]	1.0 (1) [9]			
	Day 3 of lactation	1.0 (1) [11]	1.0 (1)	1.0 (1) [11]	1.0 (1) [9]			

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		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		
Open-field test										
Consciousness	Pre	2.0	(2)	2.0	(2)	2.0	(2)	2.0	(2)	
	Mean (range)	2.0	(2)	2.0	(2)	2.0	(2)	2.0	(2)	
Behavioral abnormalities	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)	[11]
	Day 1 of pregnancy	2.0	(2)	[11]	2.0	(2)	[11]	2.0	(2)	[10]
	Day 8 of pregnancy	2.0	(2)	[11]	2.0	(2)	[11]	2.0	(2)	[10]
	Day 15 of pregnancy	2.0	(2)	[11]	2.0	(2)	[11]	2.0	(2)	[10]
	Day 3 of lactation	2.0	(2)	[11]	2.0	(2)	[11]	2.0	(2)	[9]
	Mean (range)	1.0	(1)		1.0	(1)		1.0	(1)	
Righting reflex	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)	[11]
	Day 1 of pregnancy	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1)	[10]
	Day 8 of pregnancy	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1)	[10]
	Day 15 of pregnancy	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1)	[10]
	Day 3 of lactation	1.0	(1)	[11]	1.0	(1)	[11]	1.0	(1)	[9]

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 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		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					
Posture	Pre	2.0 (2)	2.0 (2)	2.0 (2)	
	Mean (range)				
Mean (range)	Day 8	2.0 (2)	2.0 (2)	2.0 (2)	
	Day 15	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 22	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 29	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 36	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 42	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 42	2.0 (2)	2.0 (2)	2.0 (2)	[5]
Palpebral closure	Pre	1.0 (1)	1.0 (1)	1.0 (1)	
	Mean (range)				
Mean (range)	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]
	Day 42	1.0 (1)	1.0 (1)	1.0 (1)	[5]
Biting behavior	Pre	1.0 (1)	1.0 (1)	1.0 (1)	
	Mean (range)				
Mean (range)	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]
	Day 42	1.0 (1)	1.0 (1)	1.0 (1)	[5]
Clonic convulsions	Pre	1.0 (1)	1.0 (1)	1.0 (1)	
	Mean (range)				
Mean (range)	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]
	Day 42	1.0 (1)	1.0 (1)	1.0 (1)	[5]

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	720
Number of females		6	6	6
Observation of animals in cages				
Tonic convulsions	Pre	1.0 (1)	1.0 (1)	1.0 (1)
	Mean (range)			
	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.

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	
mg/kg		0		180	
Number of females		6		6	
Observation of animals on observer's palm					
Ease of removal from cage	Pre	2.0 (2)	2.0 (2)	2.0 (2)	
	Mean (range)				
Mean (range)	Day 8	2.0 (2)	2.0 (2)	2.0 (2)	
	Day 15	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 22	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 29	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 36	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 42	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 42	2.0 (2)	2.0 (2)	2.0 (2)	[5]
Ease of handling	Pre	2.0 (2)	2.0 (2)	2.0 (2)	
	Mean (range)				
Mean (range)	Day 8	2.0 (2)	2.0 (2)	2.0 (2)	
	Day 15	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 22	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 29	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 36	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 42	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 42	2.0 (2)	2.0 (2)	2.0 (2)	[5]
Muscle tone	Pre	2.0 (2)	2.0 (2)	2.0 (2)	
	Mean (range)				
Mean (range)	Day 8	2.0 (2)	2.0 (2)	2.0 (2)	
	Day 15	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 22	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 29	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 36	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 42	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 42	2.0 (2)	2.0 (2)	2.0 (2)	[5]
Fur conditions	Pre	1.0 (1)	1.0 (1)	1.0 (1)	
	Mean (range)				
Mean (range)	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]
	Day 42	1.0 (1)	1.0 (1)	1.0 (1)	[5]

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		Control		1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene	
mg/kg		0	180	720	
Number of females		6	6	6	
Observation of animals on observer's palm					
Lacrimation 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]
	Salivation Mean (range)	Pre	1.0 (1)	1.0 (1)	1.0 (1)
Day 8		1.0 (1)	1.0 (1)	1.8 (1-2)	**
Day 15		1.0 (1)	1.3 (1-2)	2.0 (2)	** [5]
Day 22		1.0 (1)	1.0 (1)	2.0 (2)	[5]
Day 29		1.0 (1)	1.7 (1-2) **	2.0 (2)	** [5]
Day 36		1.0 (1)	1.0 (1)	1.8 (1-2)	** [5]
Day 42		1.0 (1)	1.0 (1)	2.0 (2)	[5]
Respiration 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.

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				
mg/kg		0		180		720		
Number of females		6		6		6		
Open-field test								
Frequency of rearing	Pre	4.7 ±	2.9	5.8 ±	4.3	6.5 ±	2.3	
	Mean ± S.D.							
Mean ± S.D.	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	Pre	0.0 ±	0.0	0.0 ±	0.0	0.0 ±	0.0	
	Mean ± S.D.							
Mean ± S.D.	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	Pre	1.0	(1)	1.0	(1)	1.0	(1)	
	Mean (range)							
Mean (range)	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	Pre	1.0	(1)	1.0	(1)	1.0	(1)	
	Mean (range)							
Mean (range)	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: 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 18-6 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	720	
Number of females		6	6	6	
Open-field test					
Consciousness Mean (range)	Pre	2.0 (2)	2.0 (2)	2.0 (2)	
	Day 8	2.0 (2)	2.0 (2)	2.0 (2)	
	Day 15	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 22	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 29	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 36	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Day 42	2.0 (2)	2.0 (2)	2.0 (2)	[5]
	Behavioral abnormalities 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]
Righting reflex 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.

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		720	
mg/kg	0		45		180		720	
Number of males	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 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 mg/kg	Control	1,1'-(1,1-dimethyl-3-methylene-1,3-propanediyl)bisbenzene			
	0	45	180	720	
Number of females	6	6	6	6	6
Pupillary reflex					
Mean (range)	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)
Response to touch					
Mean (range)	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)
Pain reflex					
Mean (range)	3.0 (3)	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 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 21 Grip strength 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	720
mg/kg	0	45	180	720
Number of males	6	6	6	6
Forelimb	1052 ± 276	975 ± 328	1115 ± 242	1098 ± 208
Hindlimb	162 ± 59	103 ± 46	118 ± 31	124 ± 27

Each value shows mean (g) ± S.D.

Table 22 Grip strength 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
mg/kg	0	45	180	720	
Number of females	6	6	6	6	
Forelimb	939 ± 234	827 ± 225	904 ± 208	937 ± 88	
Hindlimb	113 ± 29	81 ± 25	76 ± 17	125 ± 59	

Each value shows mean (g) ± S.D.