

査では、ALP 活性の高値が雌、副腎重量の高値が雄で認められた。しかし、前述の変化と関連すると考えられる病理組織学的な異常所見が認められていないことから、その影響の程度としては軽度なもの、あるいは毒性学的な意義に乏しい変化と考えられる。

被験物質に起因するこれらの変化は、回復期間により対照群と同様となるか、あるいは消失し、回復傾向を示しているものと考えられる。

生殖発生毒性

性周期、交尾率、受胎率、分娩率、妊娠期間、黄体数、着床数、着床率、出産率および分娩状態の観察では被験物質に起因する変化は認められなかった。哺育の観察では、300 mg/kg 群の 1 例に分娩日における出産後の児なめおよび回集行動の欠如が認められ、死亡児が多発した。しかし、1 例だけの変化で哺育 1 日以後は哺育行動の異常はみられなかったことから、分娩日における一時的な変化で被験物質に起因しない偶発的な変化と考えられる。

病理学検査において、300 mg/kg 群の雄では精巣および精巣上体に病変がみられたが、全例が交尾し 300 mg/kg 群の 1 例を除き受胎が成立した。精巣で産生された精子は精巣上体内を移動しながら成熟し、精巣上体尾部へ到達するのに約 2 週間を要し、その後射精する。投与初期に被験物質の影響を受けた精子は、約 2 週間後の交配開始頃に射精されることになる。よって、投与終了後の病理検査では精巣および精巣上体に変化がみられたが、交尾時期の精子は被験物質の影響を受けた可能性が低かったか、あるいは影響を受けてもその程度が軽かったものと予想され、受胎には影響しなかったものと推察される。なお、精巣および精巣上体の病変程度から、交配前の投与期間を 2 週間以上とした場合には、生殖機能への何らかの影響を示す可能性は否定できない。

新生児の検査において、出産児数、出生率および新生児の 4 日生存率、さらに一般状態、外表検査、体重および剖検のいずれにも被験物質に起因する変化は認められなかった。したがって、被験物質は次世代の発生および発育へ影響を及ぼすものではないと考えられる。

以上のように、1,3-ビス(アミノメチル)シクロヘキサンを反復経口投与した結果、一般毒性学的な主な変化として、300 mg/kg 群で死亡が雄 1 例、体重増加の抑制が雄、流涎が雌雄、病理学検査では同群において前胃への影響が雌雄、精巣および精巣上体への影響が認められた。これらの変化は 2 週間の回復期間により消失するか、あるいは回復傾向を示した。生殖発生毒性への影響は親動物および新生児に対しても被験物質に起因する変化は認められなかった。

したがって、本試験条件下における反復投与毒性に関する無影響量は雌雄とも 60 mg/kg/day、生殖発生毒性に関する無影響量は雌雄の親動物および児動物とも 300 mg/kg/day と考えられる。

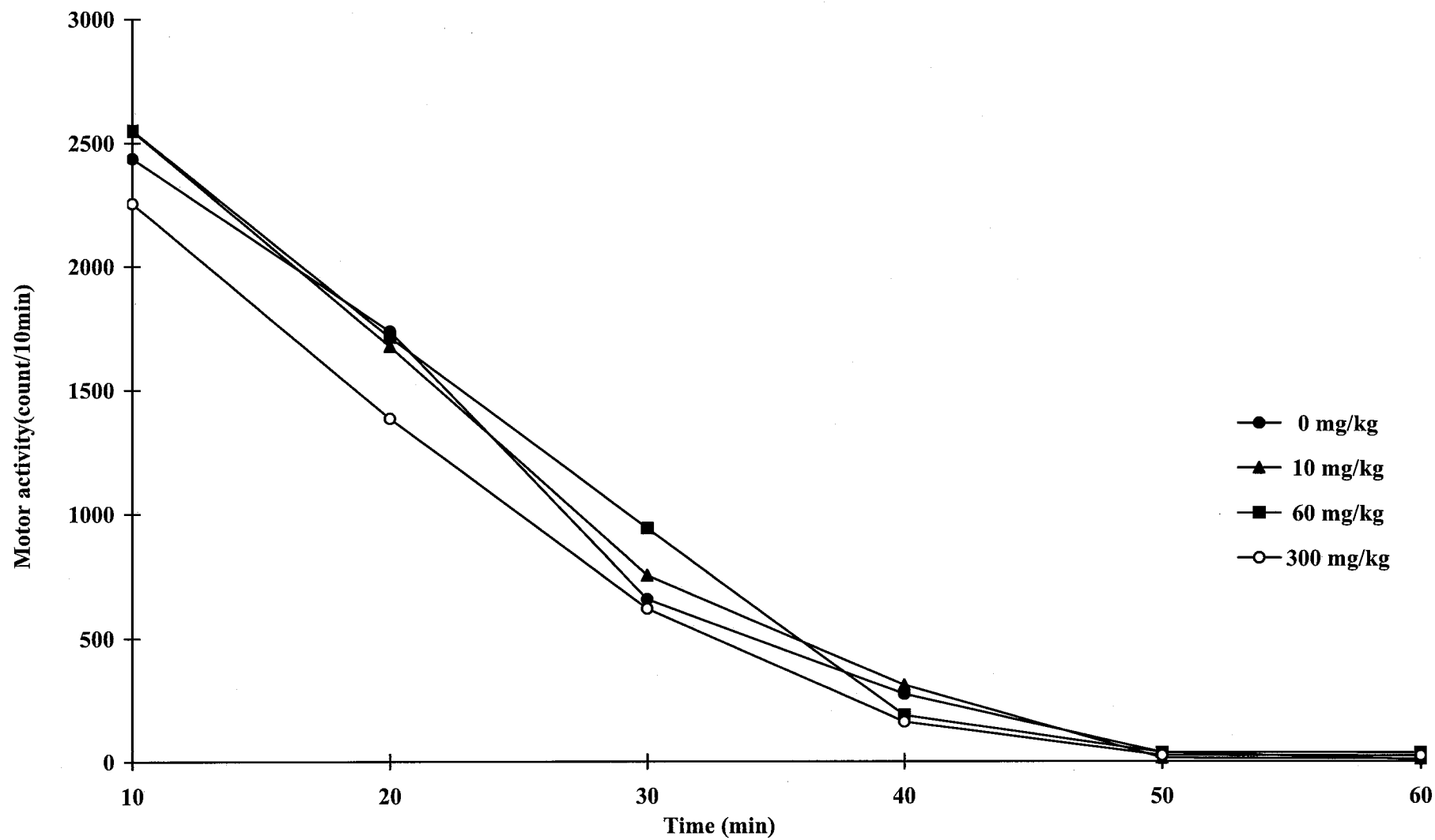


Fig.1 Motor Activity of male rats treated orally with 1,3-Bis (aminomethyl) cyclohexane in the combined repeat dose and reproductive/developmental toxicity screening test

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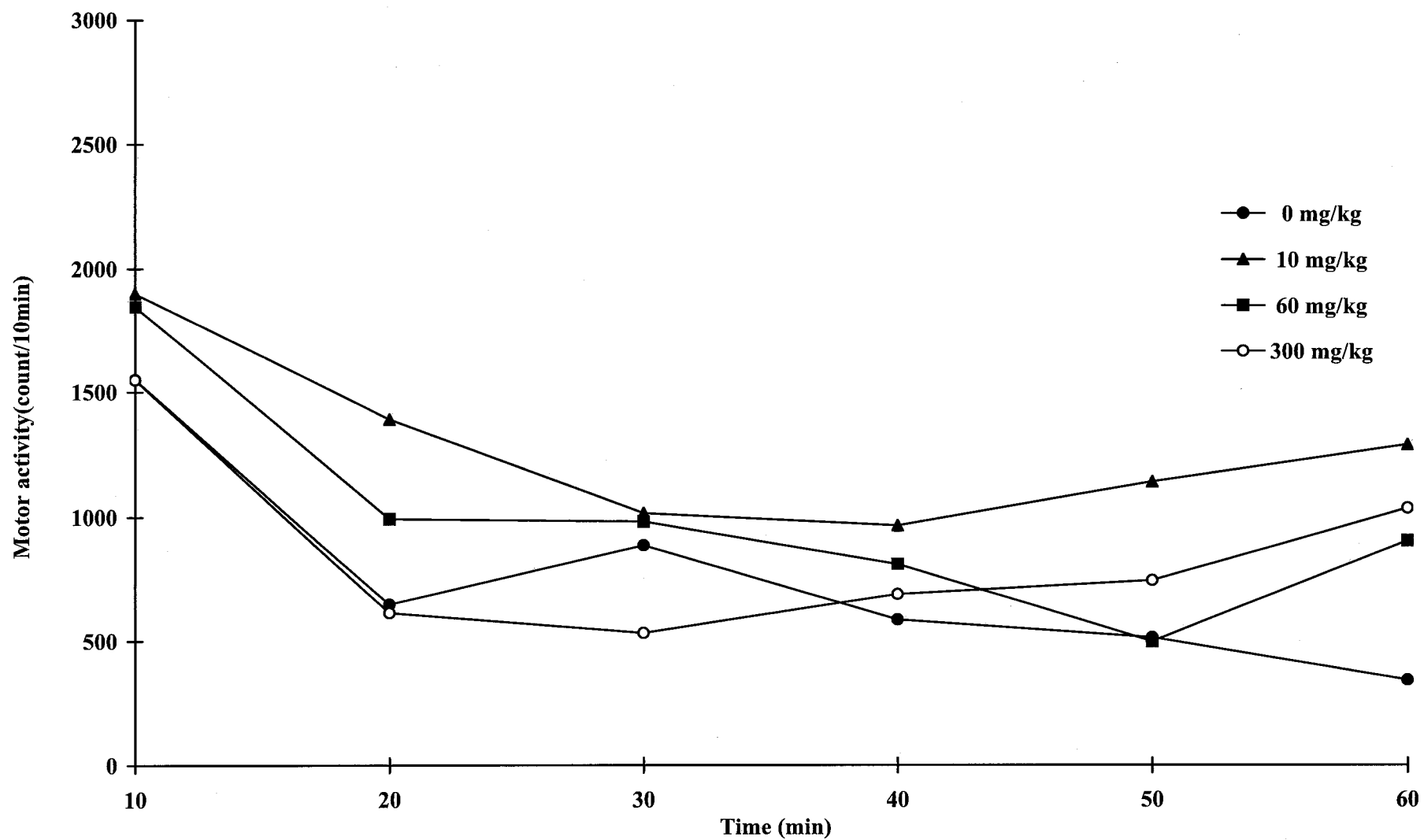


Fig.2 Motor Activity of female rats treated orally with 1,3-Bis (aminomethyl) cyclohexane in the combined repeat dose and reproductive/developmental toxicity screening test

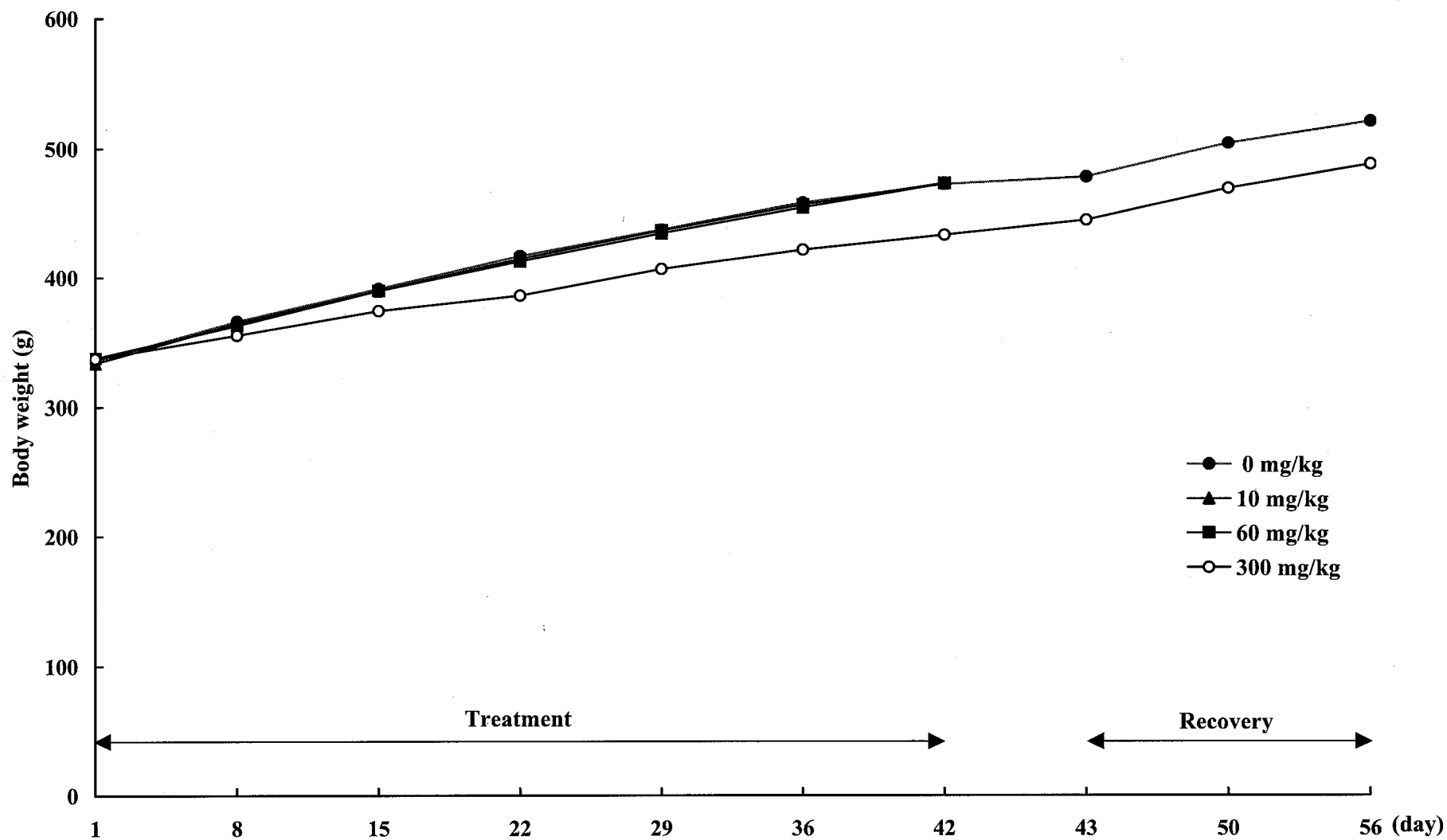


Fig.3 Body weight changes of male rats treated orally with 1,3-Bis (aminomethyl) cyclohexane in the combined repeat dose and reproductive/developmental toxicity screening test

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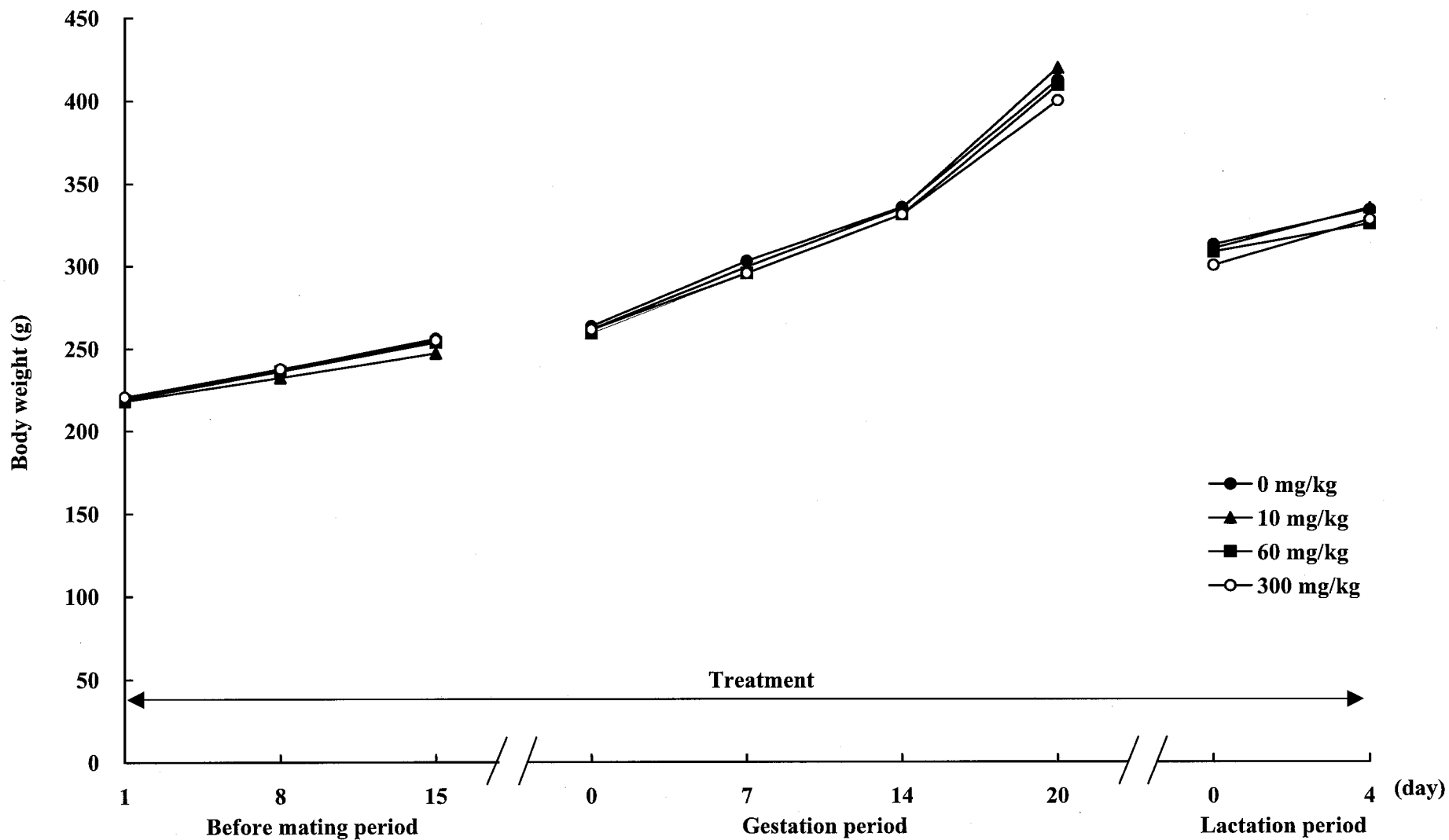


Fig.4 Body weight changes of female rats treated orally with 1,3-Bis (aminomethyl) cyclohexane in the combined repeat dose and reproductive/developmental toxicity screening test

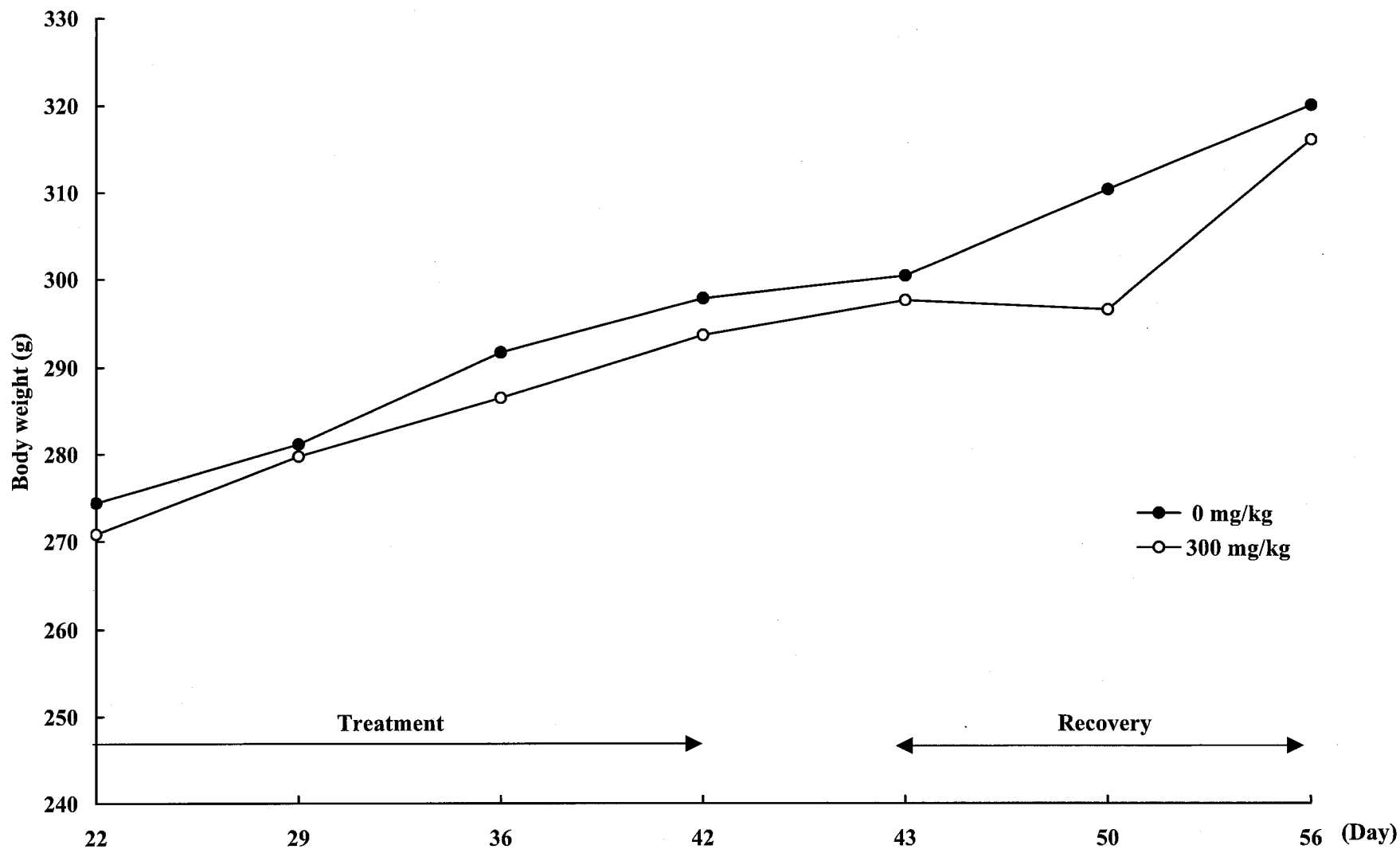


Fig.5 Body weight changes of female rats (satellite animal) treated orally with 1,3-Bis (aminomethyl) cyclohexane in the combined repeat dose and reproductive/developmental toxicity screening test

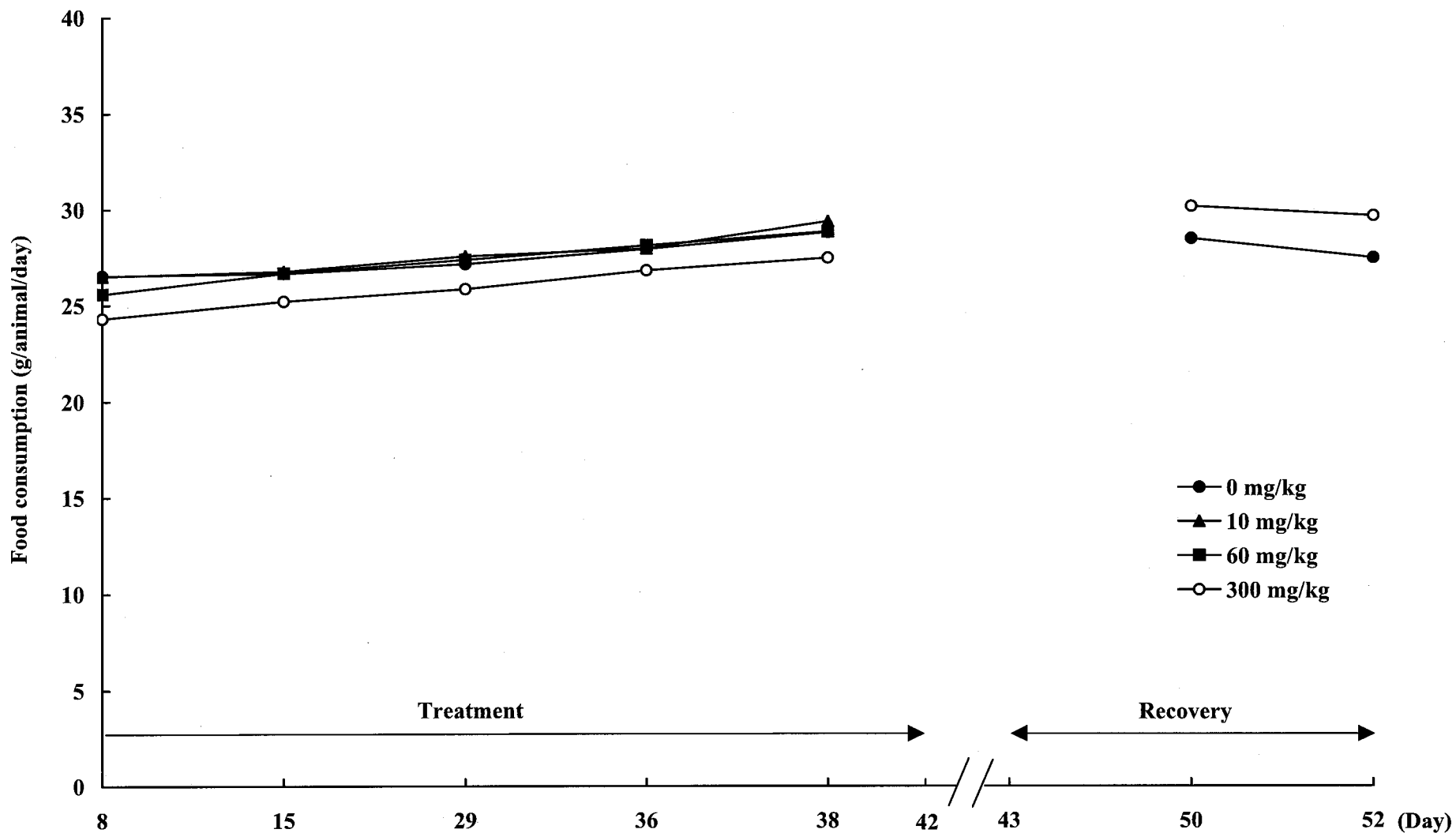


Fig.6 Food consumption of male rats treated orally with 1,3-Bis (aminomethyl) cyclohexane in the combined repeat dose and reproductive/developmental toxicity screening test

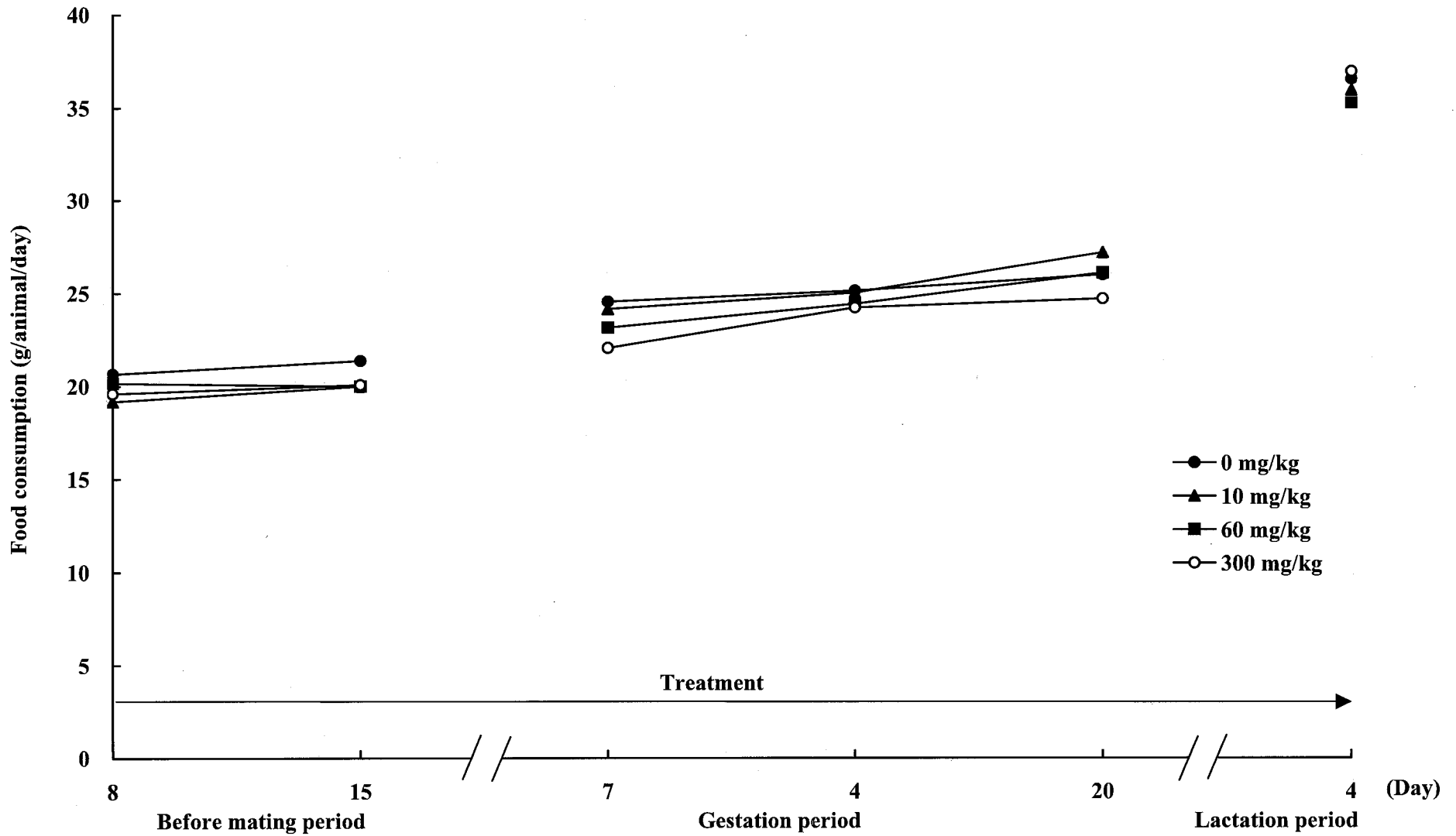


Fig.7 Food consumption of female rats treated orally with 1,3-Bis (aminomethyl) cyclohexane in the combined repeat dose and reproductive/developmental toxicity screening test

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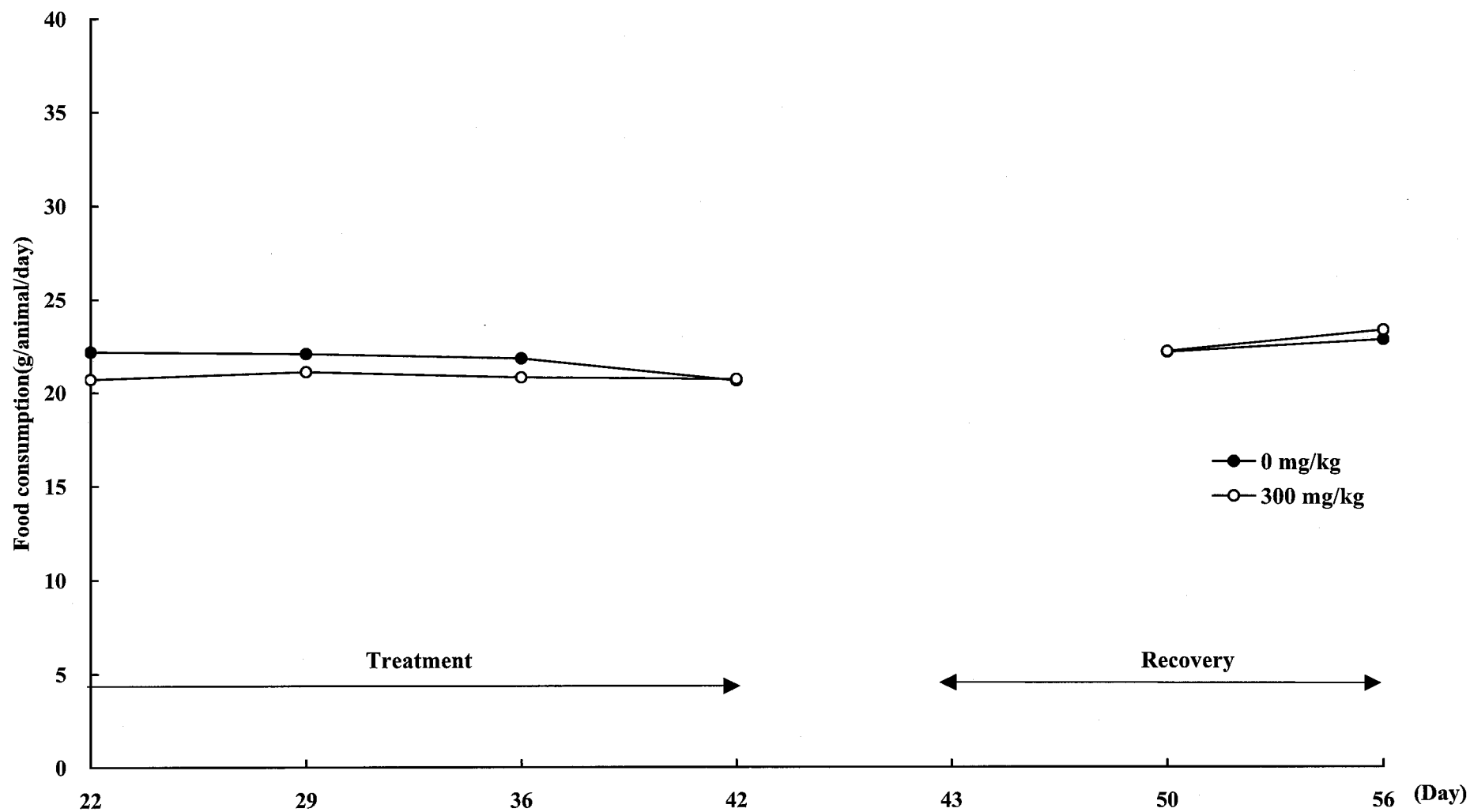


Fig.8 Food consumption of female rats (satellite animal) treated orally with 1,3-Bis (aminomethyl) cyclohexane in the combined repeat dose and reproductive/developmental toxicity screening test

Table 1 Clinical Sign - Summary

Male

Test Substance Dose(mg/kg)	Findings	Day Time	1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		
			10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20			
1, 3-BAC 0	Number of Animals		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
	No Abnormality		12	12	12	12	12	12	12	12	12	12	12	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, 3-BAC 10	Number of Animals		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No Abnormality		12	12	12	12	12	12	12	12	12	12	12	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, 3-BAC 60	Number of Animals		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No Abnormality		12	12	12	12	12	12	12	12	12	12	12	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, 3-BAC 300	Number of Animals		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No Abnormality		12	12	12	12	12	12	12	12	12	12	12	12	12	12	9	12	12	12	9	12	11	12	9	12	8	12	10	12	8	12	11	12	5	12	6
	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
	Decrease in locomotor activity	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
	Irregular respiration	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Rale	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Abnormal fur	01	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Ptosis	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
	Salivation	1	0	0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	3	0	1	0	3	0	4	0	2	0	4	0	1	0	7	0	6	

+, Present; 1, Slight; 2, Moderate; 3, Severe;
 Time 10, Before dosing; Time 20, After dosing;
 01, Whole body;

Table 1 Clinical Sign - Summary

		Male																																			
Test Substance Dose(mg/kg)	Findings	Day	18		19		20		21		22		23		24		25		26		27		28		29		30		31		32		33		34		
		Time	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20			
1, 3-BAC 0	Number of Animals		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	
	No Abnormality		12	12	12	12	12	12	12	12	12	12	12	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, 3-BAC 10	Number of Animals		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No Abnormality		12	12	12	12	12	12	12	12	12	12	12	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, 3-BAC 60	Number of Animals		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
	No Abnormality		12	12	12	12	12	12	12	12	12	12	12	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, 3-BAC 300	Number of Animals		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	
	No Abnormality		12	7	12	6	12	3	12	5	11	4	11	6	11	5	11	5	11	5	11	5	11	5	11	5	11	5	11	4	11	3	11	4	11	4	
	Death	+	0	0	0	0	0	0	0	0	0	0	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
	Decrease in locomotor activity	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Irregular respiration	+	0	0	0	0	0	0	0	0	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	0	0
	Rale	+	0	0	0	0	0	0	0	0	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	0	0
	Abnormal fur	01	+	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Ptosis		1	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Salivation		1	0	5	0	6	0	9	0	7	0	8	0	5	0	6	0	6	0	6	0	6	0	6	0	6	0	6	0	7	0	8	0	7	0	7

+, Present; 1, Slight; 2, Moderate; 3, Severe;
 Time 10, Before dosing; Time 20, After dosing;
 01, Whole body;

Table 1 Clinical Sign - Summary

Male

Test Substance Dose (mg/kg)	Findings	Day 35		36		37		38		39		40		41		42		43		44	45	46	47	48	49	50	51	52	53	54	55	56	57
		Time 10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20
1,3-BAC 0	Number of Animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	5	5	5	5	5	5	5	5	5	5	5	5	5	
	No Abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	5	5	5	5	5	5	5	5	5	5	5	5	5	
1,3-BAC 10	Number of Animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12														
	No Abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12														
1,3-BAC 60	Number of Animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12														
	No Abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12														
1,3-BAC 300	Number of Animals	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	5	5	5	5	5	5	5	5	5	5	5	5		
	No Abnormality	11	3	11	3	11	2	11	2	11	5	11	6	11	4	11	4	11	5	5	5	5	5	5	5	5	5	5	5	5	5		
	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		
	Decrease in locomotor activity	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		
	Irregular respiration	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	Rale	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	Abnormal fur	01	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
	Ptosis	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		
Salivation	1	0	8	0	8	0	9	0	9	0	6	0	5	0	7	0	7	0	0	0	0	0	0	0	0	0	0	0	0	0			

+, Present; 1, Slight; 2, Moderate; 3, Severe;
 Time 10, Before dosing; Time 20, After dosing;
 01, Whole body;

Table 2 Clinical Sign - Summary

Test Substance Dose (mg/kg)	Findings	Day Time	Female																																
			1		2		3		4		5		6		7		8		9		10		11		12		13		14		15				
			10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20			
1, 3-BAC 0	Number of Animals		17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17				
	No Abnormality		17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17			
1, 3-BAC 10	Number of Animals		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12				
	No Abnormality		12	12	12	12	12	12	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, 3-BAC 60	Number of Animals		12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12				
	No Abnormality		12	12	12	12	12	12	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, 3-BAC 300	Number of Animals		17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17				
	No Abnormality		17	17	17	17	17	17	17	17	17	17	17	17	17	16	17	15	17	13	17	14	17	13	17	13	17	14	17	12	17	12			
	Salivation	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	2	0	4	0	3	0	4	0	4	0	3	0	5	0

+, Present; 1, Slight; 2, Moderate; 3, Severe;
 Time 10, Before dosing; Time 20, After dosing;

Table 3 Clinical Sign - Summary Female (Mating period)

Test Substance Dose (mg/kg)	Findings	Day Time	16		17		18		19		20		21		22		23		24		25		26		27		28		
			10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10
1, 3-BAC 0	Number of Animals		7	7	4	4	4	4																					
	No Abnormality		7	7	4	4	4	4																					
1, 3-BAC 10	Number of Animals		10	10	8	8	4	4	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
	No Abnormality		10	10	8	8	4	4	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
1, 3-BAC 60	Number of Animals		9	9	4	4	2	2																					
	No Abnormality		9	9	4	4	2	2																					
1, 3-BAC 300	Number of Animals		11	11	8	8	3	3	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
	No Abnormality		11	5	8	5	3	1	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
	Salivation			6		3		2																					

+, Present; 1, Slight; 2, Moderate; 3, Severe;
Time 10, Before dosing; Time 20, After dosing;

Table 4

Study No. B041798

Clinical Sign (FO Gestation) - Summary
 Sex : Female Time 10 : Before dosing

Test Substance Dose (mg/kg)	Findings	/Day																						
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
1, 3-BAC 0	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	5
	No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	5
1, 3-BAC 10	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	5
	No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	5
1, 3-BAC 60	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	6
	No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	6
1, 3-BAC 300	Number of animals	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	6
	No abnormality Rate	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	10	11	6
																						1		

Table 4
Table Continued

Study No. B041798

Clinical Sign (F0 Gestation) - Summary
Sex : Female Time 20 : After dosing

Test Substance Dose(mg/kg)	Findings	/Day																						
		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
1, 3-BAC 0	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	5
	No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	5
1, 3-BAC 10	Number of animals	11	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	5
	No abnormality	11	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	5
1, 3-BAC 60	Number of animals	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	6
	No abnormality	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	6
1, 3-BAC 300	Number of animals	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	11	6
	No abnormality	8	8	8	7	10	8	8	6	7	10	9	7	10	9	8	6	7	6	7	8	6	5	3
	Decrease in locomotor activity															1			1	1	1	1		
	Rale																							
	Salivation	3	3	3	4	1	3	3	5	4	1	2	4	1	2	3	1	4	5	1	1	5	3	

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Table 5

Study No. B041798

Clinical Sign (F0 Lactation) - Summary
 Sex : Female Time 10 : Before dosing

Test Substance Dose (mg/kg)	Findings	/Day					
		0	1	2	3	4	5
1, 3-BAC 0	Number of animals	12	12	12	12	12	12
	No abnormality	12	12	12	12	12	12
1, 3-BAC 10	Number of animals	12	12	12	12	12	12
	No abnormality	12	12	12	12	12	12
1, 3-BAC 60	Number of animals	12	12	12	12	12	12
	No abnormality	12	12	12	12	12	12
1, 3-BAC 300	Number of animals	11	11	11	11	11	11
	No abnormality	10	11	11	11	11	11
	Loss of licking pups	1					
	Loss of retrieving	1					

Table 5
Table Continued

Clinical Sign (F0 Lactation) - Summary
Sex : Female Time 20 : After dosing

Test Substance Dose (mg/kg)	Findings	/Day				
		0	1	2	3	4
1, 3-BAC 0	Number of animals	12	12	12	12	12
	No abnormality	12	12	12	12	12
1, 3-BAC 10	Number of animals	12	12	12	12	12
	No abnormality	12	12	12	12	12
1, 3-BAC 60	Number of animals	12	12	12	12	12
	No abnormality	12	12	12	12	12
1, 3-BAC 300	Number of animals	11	11	11	11	11
	No abnormality	4	9	7	7	9
	Decrease in locomotor activity	1	1			
	Salivation	7	2	4	4	2
	Loss of licking pups	1				
	Loss of retrieving	1				

Table 6 Clinical Sign - Summary

Female #

Test Substance Dose (mg/kg)	Findings	Day 16		17		18		19		20		21		22		23		24		25		26		27		28		29		30		31		32	
		Time 10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20		
1,3-BAC 0	Number of Animals	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	5	5	5	5	5	5	5		
	No Abnormality	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	5	5	5	5	5	5	5		
	Loss of teeth	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
1,3-BAC 300	Number of Animals	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	5	5	5	5	5	5			
	No Abnormality	5	4	5	4	5	3	5	4	5	3	5	3	5	3	5	3	5	4	5	4	5	5	5	2	5	3	5	2	5	2	5	2		
	Salivation	1	0	1	0	1	0	2	0	1	0	2	0	2	0	2	0	2	0	1	0	1	0	0	3	0	2	0	3	0	3	0	3		

+, Present; 1, Slight; 2, Moderate; 3, Severe;
 Time 10, Before dosing; Time 20, After dosing;
 #:Satellite animal

Table 6 Clinical Sign - Summary

Test Substance Dose (mg/kg)	Findings	Day Time	Female #																																	
			33 10	33 20	34 10	34 20	35 10	35 20	36 10	36 20	37 10	37 20	38 10	38 20	39 10	39 20	40 10	40 20	41 10	41 20	42 10	42 20	43	44	45	46	47	48	49	50	51	52	53	54	55	56
1,3-BAC 0	Number of Animals		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	5	5	5	5	5	5	5	5	
	No Abnormality		5	5	5	5	5	5	5	5	5	5	5	5	5	5	4	4	4	4	4	4	5	5	5	5	5	5	5	5	5	5	5	5	5	
	Loss of teeth	+	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	
1,3-BAC 300	Number of Animals		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	5	5	5	5	5	5	5	5	
	No Abnormality		5	4	5	2	5	3	5	2	5	2	5	1	5	3	5	3	5	3	5	4	5	5	5	5	5	5	5	5	5	5	5	5	5	5
	Salivation	1	0	1	0	3	0	2	0	3	0	3	0	4	0	2	0	2	0	2	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0

+, Present; 1, Slight; 2, Moderate; 3, Severe;
 Time 10, Before dosing; Time 20, After dosing;
 #: Satellite animal

Table 6 Clinical Sign - Summary

Female #

Study No. B041798

Test Substance Dose (mg/kg)	Findings	Day	57
1, 3-BAC 0	Number of Animals		5
	No Abnormality		5
	Loss of teeth	+	0
1, 3-BAC 300	Number of Animals		5
	No Abnormality		5
	Salivation	1	0

+, Present; 1, Slight; 2, Moderate; 3, Severe;

#: Satellite animal

Table 7 Detailed Clinical Observations - Summary (Week -1)

Items	Sex: Test Substance: Dose (mg/kg): Number of Animals:	Male				Female			
		1, 3-BAC	1, 3-BAC	1, 3-BAC	1, 3-BAC	1, 3-BAC	1, 3-BAC	1, 3-BAC	1, 3-BAC
		0	10	60	300	0	10	60	300
		12	12	12	12	17	12	12	17
Home cage observations	(Criteria)								
Tremor	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Clonic convulsion	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Tonic convulsion	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Breathing	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
Hand-held observations									
Reactivity on removal	1	0	0	0	0	0	0	0	0
from the cage	2	12	12	12	12	17	12	12	17
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0	0
	6	0	0	0	0	0	0	0	0

See Annex 12.7 for details of criteria.

Table 7 Detailed Clinical Observations - Summary (Week -1)

Items	Sex: Test Substance: Dose (mg/kg): Number of Animals:	Male				Female			
		1, 3-BAC	1, 3-BAC	1, 3-BAC	1, 3-BAC	1, 3-BAC	1, 3-BAC	1, 3-BAC	1, 3-BAC
		0	10	60	300	0	10	60	300
		12	12	12	12	17	12	12	17
Hand-held observations	(Criteria)								
Reactivity to handling	1	0	0	0	0	0	0	0	0
	2	12	12	12	12	17	12	12	17
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
Aggression	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Trauma	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Color of skin	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Soiled fur	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Exophthalmos	N	12	12	12	12	17	12	12	17
	P	0	0	0	0	0	0	0	0
Palpebral closure	1	12	12	12	12	17	12	12	17
	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0	0
Color of conjunctiva	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0
Secretion	N	12	12	12	12	17	12	12	17
	1	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0

See Annex 12.7 for details of criteria.