2,4-ペンタンジオンのマウスを用いた
吸入による 13 週間毒性試験報告書

試験番号：0601

TABLES

TABLES

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TABLE 1 CONCENTRATIONS OF 2,4-PENTANEDIONE IN THE INHALATION CHAMBER OF THE 13-WEEK INHALATION STUDY

Group Name	Concentration(ppm) Mean ± S.D.
Control	0.0 ± 0.0
25 ppm	25.6 ± 0.6
50 ppm	50.7 ± 0.8
100 ppm	101.3 ± 1.4
200 ppm	201.1 ± 2.2
400 ppm	400.2 ± 3.2

TABLE 2 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE MICE IN THE 13-WEEK INHALATION STUDY OF 2,4-PENTANEDIONE

Week on Study	Control		25 ppm			50 ppm			100 ppm			200 ppm			400 ppm		
	Av. Wt.	No. of Surviv. <10>	Av. Wt.	% of cont.	No. of Surviv. <10>	Av. Wt.	% of cont.	No. of Surviv. <10>	Av. Wt.	% of cont.	No. of Surviv. <10>	Av. Wt.	% of cont.	No. of Surviv. <10>	Av. Wt.	% of cont.	No. of Surviv. <10>
0	24.0 (10)	10 / 10	24.0 (10)	100	10 / 10	24.0 (10)	100	10 / 10	24.0 (10)	100	10 / 10	24.0 (10)	100	10 / 10	24.0 (10)	100	10 / 10
1	25.4 (10)	10 / 10	25.6 (10)	101	10 / 10	25.5 (10)	100	10 / 10	25.0 (10)	98	10 / 10	25.3 (10)	100	10 / 10	24.9 (10)	98	10 / 10
2	26.3 (10)	10 / 10	26.2 (10)	100	10 / 10	26.4 (10)	100	10 / 10	25.9 (10)	98	10 / 10	26.0 (10)	99	10 / 10	25.5 (10)	97	10 / 10
3	27.1 (10)	10 / 10	27.0 (10)	100	10 / 10	26.9 (10)	99	10 / 10	26.3 (10)	97	10 / 10	26.4 (10)	97	10 / 10	26.2 (10)	97	10 / 10
4	27.9 (10)	10 / 10	27.9 (10)	100	10 / 10	27.3 (10)	98	10 / 10	27.0 (10)	97	10 / 10	27.0 (10)	97	10 / 10	26.8 (10)	96	10 / 10
5	28.9 (10)	10 / 10	28.5 (10)	99	10 / 10	28.1 (10)	97	10 / 10	28.0 (10)	97	10 / 10	27.8 (10)	96	10 / 10	27.3 (10)	94	10 / 10
6	29.6 (10)	10 / 10	28.8 (10)	97	10 / 10	28.6 (10)	97	10 / 10	28.3 (10)	96	10 / 10	28.1 (10)	95	10 / 10	28.0 (10)	95	10 / 10
7	30.2 (10)	10 / 10	29.4 (10)	97	10 / 10	28.9 (10)	96	10 / 10	28.7 (10)	95	10 / 10	28.3 (10)	94	10 / 10	28.3 (10)	94	10 / 10
8	31.3 (10)	10 / 10	30.3 (10)	97	10 / 10	29.8 (10)	95	10 / 10	29.3 (10)	94	10 / 10	29.2 (10)	93	10 / 10	29.2 (10)	93	10 / 10
9	32.0 (10)	10 / 10	31.1 (10)	97	10 / 10	30.6 (10)	96	10 / 10	29.8 (10)	93	10 / 10	30.1 (10)	94	10 / 10	30.2 (10)	94	10 / 10
10	32.9 (10)	10 / 10	31.5 (10)	96	10 / 10	31.3 (10)	95	10 / 10	30.4 (10)	92	10 / 10	31.5 (10)	96	10 / 10	30.7 (10)	93	10 / 10
11	33.3 (10)	10 / 10	32.3 (10)	97	10 / 10	31.9 (10)	96	10 / 10	31.3 (10)	94	10 / 10	32.0 (10)	96	10 / 10	31.1 (10)	93	10 / 10
12	34.4 (10)	10 / 10	32.9 (10)	96	10 / 10	32.7 (10)	95	10 / 10	31.7 (10)	92	10 / 10	32.6 (10)	95	10 / 10	31.8 (10)	92	10 / 10
13	34.5 (10)	10 / 10	33.3 (10)	97	10 / 10	32.3 (10)	94	10 / 10	32.1 (10)	93	10 / 10	33.1 (10)	96	10 / 10	31.9 (10)	92	10 / 10

< > : No. of effective animals, ( ) : No. of measured animals, Av. Wt. : Averaged body weight (Unit : g).

TABLE 3 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF FEMALE MICE IN THE 13-WEEK INHALATION STUDY OF 2,4-PENTANEDIONE

Week on Study	Control		25 ppm			50 ppm			100 ppm			200 ppm			400 ppm		
	Av. Wt.	No. of Surviv. <10>	Av. Wt.	% of cont.	No. of Surviv. <10>	Av. Wt.	% of cont.	No. of Surviv. <10>	Av. Wt.	% of cont.	No. of Surviv. <10>	Av. Wt.	% of cont.	No. of Surviv. <10>	Av. Wt.	% of cont.	No. of Surviv. <10>
0	19.6 (10)	10 / 10	19.6 (10)	100	10 / 10	19.6 (10)	100	10 / 10	19.6 (10)	100	10 / 10	19.6 (10)	100	10 / 10	19.6 (10)	100	10 / 10
1	20.3 (10)	10 / 10	20.3 (10)	100	10 / 10	20.5 (10)	101	10 / 10	20.2 (10)	100	10 / 10	20.2 (10)	100	10 / 10	19.8 (10)	98	10 / 10
2	21.3 (10)	10 / 10	21.2 (10)	100	10 / 10	21.1 (10)	99	10 / 10	21.2 (10)	100	10 / 10	21.2 (10)	100	10 / 10	20.4 (10)	96	10 / 10
3	22.3 (10)	10 / 10	21.7 (10)	97	10 / 10	22.6 (10)	101	10 / 10	22.3 (10)	100	10 / 10	22.2 (10)	100	10 / 10	21.6 (10)	97	10 / 10
4	22.7 (10)	10 / 10	22.7 (10)	100	10 / 10	23.2 (10)	102	10 / 10	22.8 (10)	100	10 / 10	22.9 (10)	101	10 / 10	22.1 (10)	97	10 / 10
5	23.1 (10)	10 / 10	23.2 (10)	100	10 / 10	24.1 (10)	104	10 / 10	23.5 (10)	102	10 / 10	23.8 (10)	103	10 / 10	22.8 (10)	99	10 / 10
6	24.2 (10)	10 / 10	23.9 (10)	99	10 / 10	24.7 (10)	102	10 / 10	24.2 (10)	100	10 / 10	24.4 (10)	101	10 / 10	23.3 (10)	96	10 / 10
7	24.5 (10)	10 / 10	23.9 (10)	98	10 / 10	25.2 (10)	103	10 / 10	24.7 (10)	101	10 / 10	24.3 (10)	99	10 / 10	23.7 (10)	97	10 / 10
8	24.8 (10)	10 / 10	25.1 (10)	101	10 / 10	25.6 (10)	103	10 / 10	24.7 (10)	100	10 / 10	25.1 (10)	101	10 / 10	24.1 (10)	97	10 / 10
9	25.0 (10)	10 / 10	25.2 (10)	101	10 / 10	25.8 (10)	103	10 / 10	25.1 (10)	100	10 / 10	25.4 (10)	102	10 / 10	24.4 (10)	98	10 / 10
10	25.2 (10)	10 / 10	25.5 (10)	101	10 / 10	25.8 (10)	102	10 / 10	25.9 (10)	103	10 / 10	26.0 (10)	103	10 / 10	24.6 (10)	98	10 / 10
11	25.9 (10)	10 / 10	25.5 (10)	98	10 / 10	26.5 (10)	102	10 / 10	26.6 (10)	103	10 / 10	26.8 (10)	103	10 / 10	25.2 (10)	97	10 / 10
12	26.4 (10)	10 / 10	26.0 (10)	98	10 / 10	27.1 (10)	103	10 / 10	26.2 (10)	99	10 / 10	26.5 (10)	100	10 / 10	25.8 (10)	98	10 / 10
13	26.6 (10)	10 / 10	26.4 (10)	99	10 / 10	26.9 (10)	101	10 / 10	26.8 (10)	101	10 / 10	27.0 (10)	102	10 / 10	25.6 (10)	96	10 / 10

< > : No. of effective animals, ( ) : No. of measured animals, Av. Wt. : Averaged body weight (Unit : g).

TABLE 4 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 13-WEEK INHALATION STUDY OF 2,4-PENTANEDIONE

Week on Study	Control		25 ppm			50 ppm			100 ppm			200 ppm			400 ppm		
	Av. FC.	No. of Surviv.	Av. FC.	% of cont.	No. of Surviv.	Av. FC.	% of cont.	No. of Surviv.	Av. FC.	% of cont.	No. of Surviv.	Av. FC.	% of cont.	No. of Surviv.	Av. FC.	% of cont.	No. of Surviv.
	<10>		<10>			<10>			<10>			<10>			<10>		
1	4.3 (10)	10 / 10	4.5 (10)	105	10 / 10	4.5 (10)	105	10 / 10	4.3 (10)	100	10 / 10	4.5 (10)	105	10 / 10	4.3 (10)	100	10 / 10
2	4.1 (10)	10 / 10	4.2 (10)	102	10 / 10	4.4 (10)	107	10 / 10	4.3 (10)	105	10 / 10	4.3 (10)	105	10 / 10	4.1 (10)	100	10 / 10
3	4.4 (10)	10 / 10	4.4 (10)	100	10 / 10	4.5 (10)	102	10 / 10	4.5 (10)	102	10 / 10	4.6 (10)	105	10 / 10	4.4 (10)	100	10 / 10
4	4.4 (10)	10 / 10	4.5 (10)	102	10 / 10	4.6 (10)	105	10 / 10	4.7 (10)	107	10 / 10	4.6 (10)	105	10 / 10	4.5 (10)	102	10 / 10
5	4.4 (10)	10 / 10	4.4 (10)	100	10 / 10	4.6 (10)	105	10 / 10	4.7 (10)	107	10 / 10	4.5 (10)	102	10 / 10	4.3 (10)	98	10 / 10
6	4.4 (10)	10 / 10	4.7 (10)	107	10 / 10	4.8 (10)	109	10 / 10	4.9 (10)	111	10 / 10	4.7 (10)	107	10 / 10	4.6 (10)	105	10 / 10
7	4.4 (10)	10 / 10	4.6 (10)	105	10 / 10	4.8 (10)	109	10 / 10	4.9 (10)	111	10 / 10	4.6 (10)	105	10 / 10	4.5 (10)	102	10 / 10
8	4.7 (10)	10 / 10	4.8 (10)	102	10 / 10	5.0 (10)	106	10 / 10	5.0 (10)	106	10 / 10	5.0 (10)	106	10 / 10	4.7 (10)	100	10 / 10
9	4.6 (10)	10 / 10	4.8 (10)	104	10 / 10	5.0 (10)	109	10 / 10	5.0 (10)	109	10 / 10	5.0 (10)	109	10 / 10	4.9 (10)	107	10 / 10
10	4.8 (10)	10 / 10	4.8 (10)	100	10 / 10	5.1 (10)	106	10 / 10	5.2 (10)	108	10 / 10	5.1 (10)	106	10 / 10	4.8 (10)	100	10 / 10
11	4.8 (10)	10 / 10	4.9 (10)	102	10 / 10	5.1 (10)	106	10 / 10	5.3 (10)	110	10 / 10	5.1 (10)	106	10 / 10	4.8 (10)	100	10 / 10
12	4.8 (10)	10 / 10	4.9 (10)	102	10 / 10	5.2 (10)	108	10 / 10	5.2 (10)	108	10 / 10	5.2 (10)	108	10 / 10	4.9 (10)	102	10 / 10
13	4.7 (10)	10 / 10	4.8 (10)	102	10 / 10	4.7 (10)	100	10 / 10	4.9 (10)	104	10 / 10	5.0 (10)	106	10 / 10	4.7 (10)	100	10 / 10

< > : No. of effective animals, ( ) : No. of measured animals, Av. FC. : Averaged food consumption (Unit : g).

TABLE 5 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 13-WEEK INHALATION STUDY OF 2,4-PENTANEDIONE

Week on Study	Control		25 ppm			50 ppm			100 ppm			200 ppm			400 ppm		
	Av. FC.	No. of Surviv.	Av. FC.	% of cont.	No. of Surviv.	Av. FC.	% of cont.	No. of Surviv.	Av. FC.	% of cont.	No. of Surviv.	Av. FC.	% of cont.	No. of Surviv.	Av. FC.	% of cont.	No. of Surviv.
	<10>		<10>			<10>			<10>			<10>			<10>		
1	3.5 (10)	10 / 10	3.6 (10)	103	10 / 10	3.7 (10)	106	10 / 10	3.6 (10)	103	10 / 10	3.6 (10)	103	10 / 10	3.4 (10)	97	10 / 10
2	3.8 (10)	10 / 10	3.8 (10)	100	10 / 10	3.8 (10)	100	10 / 10	3.9 (10)	103	10 / 10	3.9 (10)	103	10 / 10	3.7 (10)	97	10 / 10
3	4.1 (10)	10 / 10	4.1 (10)	100	10 / 10	4.3 (10)	105	10 / 10	4.1 (10)	100	10 / 10	4.2 (10)	102	10 / 10	3.9 (10)	95	10 / 10
4	4.2 (10)	10 / 10	4.2 (10)	100	10 / 10	4.5 (10)	107	10 / 10	4.2 (10)	100	10 / 10	4.3 (10)	102	10 / 10	4.1 (10)	98	10 / 10
5	4.4 (10)	10 / 10	4.2 (10)	95	10 / 10	4.6 (10)	105	10 / 10	4.4 (10)	100	10 / 10	4.4 (10)	100	10 / 10	4.2 (10)	95	10 / 10
6	4.8 (10)	10 / 10	4.5 (10)	94	10 / 10	4.9 (10)	102	10 / 10	4.7 (10)	98	10 / 10	4.5 (10)	94	10 / 10	4.3 (10)	90	10 / 10
7	4.6 (10)	10 / 10	4.4 (10)	96	10 / 10	4.9 (10)	107	10 / 10	4.9 (10)	107	10 / 10	4.4 (10)	96	10 / 10	4.5 (10)	98	10 / 10
8	4.8 (10)	10 / 10	4.8 (10)	100	10 / 10	5.0 (10)	104	10 / 10	4.9 (10)	102	10 / 10	4.8 (10)	100	10 / 10	4.6 (10)	96	10 / 10
9	4.8 (10)	10 / 10	4.6 (10)	96	10 / 10	5.0 (10)	104	10 / 10	4.9 (10)	102	10 / 10	4.7 (10)	98	10 / 10	4.5 (10)	94	10 / 10
10	4.8 (10)	10 / 10	4.7 (10)	98	10 / 10	5.0 (10)	104	10 / 10	5.0 (10)	104	10 / 10	4.8 (10)	100	10 / 10	4.7 (10)	98	10 / 10
11	5.1 (10)	10 / 10	4.6 (10)	90	10 / 10	5.2 (10)	102	10 / 10	5.1 (10)	100	10 / 10	4.8 (10)	94	10 / 10	4.6 (10)	90	10 / 10
12	5.0 (10)	10 / 10	4.7 (10)	94	10 / 10	5.2 (10)	104	10 / 10	5.0 (10)	100	10 / 10	4.9 (10)	98	10 / 10	4.8 (10)	96	10 / 10
13	4.9 (10)	10 / 10	4.7 (10)	96	10 / 10	4.9 (10)	100	10 / 10	5.0 (10)	102	10 / 10	4.8 (10)	98	10 / 10	4.6 (10)	94	10 / 10

< > : No. of effective animals, ( ) : No. of measured animals, Av. FC. : Averaged food consumption (Unit : g).

TABLE 6　HEMATOLOGY OF MALE MICE IN THE 13-WEEK INHALATION STUDY OF 2,4-PENTANEDIONE

Group Name	Control	25 ppm	50 ppm	100 ppm	200 ppm	400 ppm	
No. of examined animals	10	10	10	10	9	10	
RETICULOCYTE (%)	2.0 ± 0.1	2.1 ± 0.2	1.9 ± 0.5	2.2 ± 0.2	2.1 ± 0.2	2.3 ± 0.2	**

Mean ± S.D.
Significant difference:　* : p≦0.05　** : p≦0.01　Test of Dunnett

TABLE 7　BIOCHEMISTRY OF MALE MICE IN THE 13-WEEK INHALATION STUDY OF 2,4-PENTANEDIONE

Group Name	Control	25 ppm		50 ppm		100 ppm		200 ppm		400 ppm	
No. of examined animals	10	10		10		10		10		10	
T-CHOLESTEROL (mg/dL)	91 ± 12	75 ± 13	**	74 ± 6	**	68 ± 7	**	76 ± 7	**	74 ± 9	**
TRIGLYCERIDE (mg/dL)	48 ± 17	28 ± 15	**	27 ± 11	**	23 ± 9	**	31 ± 12	*	24 ± 7	**
PHOSPHOLIPID (mg/dL)	177 ± 19	151 ± 21	**	143 ± 21	**	141 ± 11	**	151 ± 16	**	149 ± 14	**
CALCIUM (mg/dL)	8.8 ± 0.2	8.7 ± 0.2		8.8 ± 0.3		8.6 ± 0.1		8.6 ± 0.2		8.5 ± 0.2	*

Mean ± S.D.
Significant difference:　* : p≦0.05　** : p≦0.01　Test of Dunnett

TABLE 8 URINALYSIS OF MALE MICE IN THE 13-WEEK INHALATION STUDY OF 2,4-PENTANEDIONE

Group Name		Control	25 ppm	50 ppm	100 ppm	200 ppm	400 ppm
No. of examined animals		10	10	10	10	10	10
	Grade						
pH	5.0	0	0	0	0	0	0
	6.0	2	0	0	0	1	0
	6.5	0	0	2	0	0	1
	7.0	0	0	0	0	0	0
	7.5	2	2	1	2	2	2
	8.0	2	8	4	3	5	6
	8.5	4	0	3	5	2	1
	Chi square test		*				

Significant difference: * : p≦0.05 ** : p≦0.01

TABLE 9 URINALYSIS OF FEMALE MICE IN THE 13-WEEK INHALATION STUDY OF 2,4-PENTANEDIONE

Group Name		Control	25 ppm	50 ppm	100 ppm	200 ppm	400 ppm
No. of examined animals		10	10	10	10	10	10
	Grade						
Protein	−	0	0	0	0	0	0
	±	2	6	6	8	6	9
	+	8	4	4	2	4	1
	2+	0	0	0	0	0	0
	3+	0	0	0	0	0	0
	4+	0	0	0	0	0	0
	Chi square test				**		**
Ketone body	−	2	6	7	7	8	10
	±	1	4	3	1	2	0
	+	7	0	0	2	0	0
	2+	0	0	0	0	0	0
	3+	0	0	0	0	0	0
	4+	0	0	0	0	0	0
	Chi square test		**	**		**	**

Significant difference: * : p≦0.05 ** : p≦0.01

TABLE 10 INCIDENCES OF SELECTED LESIONS OF FEMALE MICE IN THE 13-WEEK INHALATION STUDY OF 2,4-PENTANEDIONE

Group Name	Control				25 ppm				50 ppm				100 ppm				200 ppm				400 ppm			
Number of examined animals	10				10				10				10				10				10			
Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
nasal cavit	<10>				<10>				<10>				<10>				<10>				<10>			
vacuolic change:olfactory epithelium	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< > : Number of animals examined at the site
Significant difference : * : p≦ 0.05 ** : p≦ 0.01 Test of Chi Square