

プロピオノニトリルのラットを用いた
吸入による13週間毒性試験報告書

試験番号：0455

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TABLE 1 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE RATS IN THE 13-WEEK INHALATION STUDY OF PROPIONONITRILE

Week-Day on Study	0ppm		6ppm			12ppm			25ppm			50ppm			100ppm		
	Av.Wt.	No.of Surviv.	Av.Wt.	% of cont.	No.of Surviv.	Av.Wt.	% of cont.	No.of Surviv.	Av.Wt.	% of cont.	No.of Surviv.	Av.Wt.	% of cont.	No.of Surviv.	Av.Wt.	% of cont.	No.of Surviv.
	<10>		<10>			<10>			<10>			<10>			<10>		
0-0	123 (10)	10/10	123 (10)	100	10/10	123 (10)	100	10/10	123 (10)	100	10/10	123 (10)	100	10/10	123 (10)	100	10/10
1-7	151 (10)	10/10	151 (10)	100	10/10	149 (10)	99	10/10	149 (10)	99	10/10	150 (10)	99	10/10	138 (10)	91	10/10
2-7	179 (10)	10/10	181 (10)	101	10/10	177 (10)	99	10/10	178 (10)	99	10/10	179 (10)	100	10/10	165 (10)	92	10/10
3-7	201 (10)	10/10	204 (10)	101	10/10	197 (10)	98	10/10	202 (10)	100	10/10	203 (10)	101	10/10	186 (10)	93	10/10
4-7	221 (10)	10/10	223 (10)	101	10/10	216 (10)	98	10/10	224 (10)	101	10/10	222 (10)	100	10/10	207 (10)	94	10/10
5-7	236 (10)	10/10	237 (10)	100	10/10	231 (10)	98	10/10	239 (10)	101	10/10	238 (10)	101	10/10	222 (10)	94	10/10
6-7	251 (10)	10/10	250 (10)	100	10/10	243 (10)	97	10/10	251 (10)	100	10/10	251 (10)	100	10/10	231 (10)	92	10/10
7-7	262 (10)	10/10	262 (10)	100	10/10	256 (10)	98	10/10	263 (10)	100	10/10	264 (10)	101	10/10	245 (10)	94	10/10
8-7	275 (10)	10/10	271 (10)	99	10/10	266 (10)	97	10/10	274 (10)	100	10/10	277 (10)	101	10/10	254 (10)	92	10/10
9-7	282 (10)	10/10	282 (10)	100	10/10	275 (10)	98	10/10	283 (10)	100	10/10	286 (10)	101	10/10	261 (10)	93	10/10
10-7	291 (10)	10/10	287 (10)	99	10/10	281 (10)	97	10/10	292 (10)	100	10/10	293 (10)	101	10/10	267 (10)	92	10/10
11-7	296 (10)	10/10	291 (10)	98	10/10	285 (10)	96	10/10	295 (10)	100	10/10	296 (10)	100	10/10	271 (10)	92	10/10
12-7	300 (10)	10/10	295 (10)	98	10/10	290 (10)	97	10/10	298 (10)	99	10/10	300 (10)	100	10/10	275 (10)	92	10/10
13-7	301 (10)	10/10	300 (10)	100	10/10	291 (10)	97	10/10	298 (10)	99	10/10	304 (10)	101	10/10	277 (10)	92	10/10

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

TABLE 2 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF FEMALE RATS IN THE 13-WEEK INHALATION STUDY OF PROPIONONITRILE

Week-Day on Study	0ppm		6ppm			12ppm			25ppm			50ppm			100ppm		
	Av.Wt.	No.of Surviv.	Av.Wt.	% of cont.	No.of Surviv.	Av.Wt.	% of cont.	No.of Surviv.	Av.Wt.	% of cont.	No.of Surviv.	Av.Wt.	% of cont.	No.of Surviv.	Av.Wt.	% of cont.	No.of Surviv.
	<10>		<10>			<10>			<10>			<10>			<10>		
0-0	96 (10)	10/10	96 (10)	100	10/10	96 (10)	100	10/10	96 (10)	100	10/10	96 (10)	100	10/10	96 (10)	100	10/10
1-7	110 (10)	10/10	110 (10)	100	10/10	109 (10)	99	10/10	108 (10)	98	10/10	110 (10)	100	10/10	106 (10)	96	10/10
2-7	121 (10)	10/10	123 (10)	102	10/10	120 (10)	99	10/10	121 (10)	100	10/10	120 (10)	99	10/10	117 (10)	97	10/10
3-7	130 (10)	10/10	133 (10)	102	10/10	130 (10)	100	10/10	129 (10)	99	10/10	129 (10)	99	10/10	127 (10)	98	10/10
4-7	137 (10)	10/10	139 (10)	101	10/10	137 (10)	100	10/10	137 (10)	100	10/10	136 (10)	99	10/10	135 (10)	99	10/10
5-7	144 (10)	10/10	145 (10)	101	10/10	143 (10)	99	10/10	143 (10)	99	10/10	142 (10)	99	10/10	141 (10)	98	10/10
6-7	147 (10)	10/10	150 (10)	102	10/10	148 (10)	101	10/10	147 (10)	100	10/10	147 (10)	100	10/10	146 (10)	99	10/10
7-7	152 (10)	10/10	155 (10)	102	10/10	152 (10)	100	10/10	152 (10)	100	10/10	151 (10)	99	10/10	151 (10)	99	10/10
8-7	155 (10)	10/10	159 (10)	103	10/10	154 (10)	99	10/10	156 (10)	101	10/10	155 (10)	100	10/10	154 (10)	99	10/10
9-7	158 (10)	10/10	163 (10)	103	10/10	157 (10)	99	10/10	160 (10)	101	10/10	157 (10)	99	10/10	159 (10)	101	10/10
10-7	163 (10)	10/10	166 (10)	102	10/10	161 (10)	99	10/10	163 (10)	100	10/10	160 (10)	98	10/10	161 (10)	99	10/10
11-7	164 (10)	10/10	168 (10)	102	10/10	165 (10)	101	10/10	166 (10)	101	10/10	164 (10)	100	10/10	162 (10)	99	10/10
12-7	165 (10)	10/10	170 (10)	103	10/10	165 (10)	100	10/10	167 (10)	101	10/10	165 (10)	100	10/10	163 (10)	99	10/10
13-7	164 (10)	10/10	168 (10)	102	10/10	164 (10)	100	10/10	168 (10)	102	10/10	164 (10)	100	10/10	163 (10)	99	10/10

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

TABLE 3 FOOD CONSUMPTION CHANGES OF MALE RATS IN THE 13-WEEK INHALATION STUDY OF PROPIONONITRILE

Week-Day on Study	0ppm			6ppm			12ppm			25ppm			50ppm			100ppm		
	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>		
1-7	14.1 (10)	10/10		13.9 (10)	99	10/10	13.8 (10)	98	10/10	13.7 (10)	97	10/10	13.5 (10)	96	10/10	10.7 (10)	76	10/10
2-7	15.2 (10)	10/10		15.3 (10)	101	10/10	14.7 (10)	97	10/10	15.2 (10)	100	10/10	14.9 (10)	98	10/10	13.2 (10)	87	10/10
3-7	15.8 (10)	10/10		16.4 (10)	104	10/10	15.6 (10)	99	10/10	15.9 (10)	101	10/10	16.0 (10)	101	10/10	14.2 (10)	90	10/10
4-7	16.5 (10)	10/10		16.7 (10)	101	10/10	16.0 (10)	97	10/10	16.5 (10)	100	10/10	16.3 (10)	99	10/10	15.2 (10)	92	10/10
5-7	15.6 (10)	10/10		16.0 (10)	103	10/10	15.2 (10)	97	10/10	16.0 (10)	103	10/10	15.9 (10)	102	10/10	15.2 (10)	97	10/10
6-7	15.4 (10)	10/10		15.7 (10)	102	10/10	15.4 (10)	100	10/10	15.2 (10)	99	10/10	15.5 (10)	101	10/10	14.3 (10)	93	10/10
7-7	15.2 (10)	10/10		15.6 (10)	103	10/10	15.2 (10)	100	10/10	15.7 (10)	103	10/10	15.4 (10)	101	10/10	14.9 (10)	98	10/10
8-7	15.1 (10)	10/10		15.5 (10)	103	10/10	15.2 (10)	101	10/10	15.7 (10)	104	10/10	15.5 (10)	103	10/10	15.1 (10)	100	10/10
9-7	15.5 (10)	10/10		15.6 (10)	101	10/10	15.3 (10)	99	10/10	16.0 (10)	103	10/10	15.7 (10)	101	10/10	14.9 (10)	96	10/10
10-7	15.3 (10)	10/10		14.6 (10)	95	10/10	14.6 (10)	95	10/10	15.4 (10)	101	10/10	15.4 (10)	101	10/10	14.3 (10)	93	10/10
11-7	14.8 (10)	10/10		14.8 (10)	100	10/10	14.4 (10)	97	10/10	14.2 (10)	96	10/10	14.9 (10)	101	10/10	14.0 (10)	95	10/10
12-7	14.6 (10)	10/10		14.8 (10)	101	10/10	14.4 (10)	99	10/10	14.5 (10)	99	10/10	14.3 (10)	98	10/10	13.9 (10)	95	10/10
13-7	15.0 (10)	10/10		15.4 (10)	103	10/10	14.8 (10)	99	10/10	14.8 (10)	99	10/10	14.5 (10)	97	10/10	14.1 (10)	94	10/10

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

TABLE 4 FOOD CONSUMPTION CHANGES OF FEMALE RATS IN THE 13-WEEK INHALATION STUDY OF PROPIONONITRILE

Week-Day on Study	0ppm		6ppm			12ppm			25ppm			50ppm			100ppm		
	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>		
1-7	10.0 (10)	10/10	10.1 (10)	101	10/10	9.8 (10)	98	10/10	10.0 (10)	100	10/10	9.8 (10)	98	10/10	8.8 (10)	88	10/10
2-7	10.4 (10)	10/10	10.9 (10)	105	10/10	10.3 (10)	99	10/10	10.5 (10)	101	10/10	10.4 (10)	100	10/10	10.1 (10)	97	10/10
3-7	10.6 (10)	10/10	10.7 (10)	101	10/10	10.9 (10)	103	10/10	10.6 (10)	100	10/10	10.7 (10)	101	10/10	10.3 (10)	97	10/10
4-7	10.5 (10)	10/10	10.5 (10)	100	10/10	10.5 (10)	100	10/10	10.2 (10)	97	10/10	10.2 (10)	97	10/10	10.3 (10)	98	10/10
5-7	10.5 (10)	10/10	10.7 (10)	102	10/10	10.4 (10)	99	10/10	10.4 (10)	99	10/10	10.7 (10)	102	10/10	10.4 (10)	99	10/10
6-7	10.0 (10)	10/10	10.1 (10)	101	10/10	9.8 (10)	98	10/10	10.0 (10)	100	10/10	9.7 (10)	97	10/10	10.0 (10)	100	10/10
7-7	10.0 (10)	10/10	10.3 (10)	103	10/10	10.1 (10)	101	10/10	9.8 (10)	98	10/10	9.9 (10)	99	10/10	9.8 (10)	98	10/10
8-7	9.7 (10)	10/10	10.0 (10)	103	10/10	9.3 (10)	96	10/10	9.6 (10)	99	10/10	9.6 (10)	99	10/10	9.9 (10)	102	10/10
9-7	10.1 (10)	10/10	10.4 (10)	103	10/10	9.9 (10)	98	10/10	10.3 (10)	102	10/10	9.8 (10)	97	10/10	10.0 (10)	99	10/10
10-7	10.0 (10)	10/10	10.5 (10)	105	10/10	9.9 (10)	99	10/10	9.9 (10)	99	10/10	9.8 (10)	98	10/10	9.6 (10)	96	10/10
11-7	10.2 (10)	10/10	10.5 (10)	103	10/10	10.3 (10)	101	10/10	10.1 (10)	99	10/10	10.2 (10)	100	10/10	9.8 (10)	96	10/10
12-7	9.6 (10)	10/10	10.4 (10)	108	10/10	9.9 (10)	103	10/10	9.7 (10)	101	10/10	9.7 (10)	101	10/10	9.6 (10)	100	10/10
13-7	9.6 (10)	10/10	10.1 (10)	105	10/10	9.7 (10)	101	10/10	9.6 (10)	100	10/10	9.7 (10)	101	10/10	9.4 (10)	98	10/10

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

TABLE 5 HEMATOLOGY OF MALE RATS IN THE 13-WEEK INHALATION STUDY OF PROPIONONITRILE

Group Name	Control	6 ppm	12 ppm	25 ppm	50 ppm	100 ppm
No. of examined animals	10	10	10	10	10	10
Red blood cell ($10^6/\mu\text{L}$)	9.61 \pm 0.14	9.57 \pm 0.18	9.67 \pm 0.17	9.59 \pm 0.29	9.49 \pm 0.21	9.14 \pm 0.22 **
Hemoglobin (g/dL)	16.2 \pm 0.2	16.0 \pm 0.3	16.2 \pm 0.3	16.1 \pm 0.4	15.9 \pm 0.3	15.4 \pm 0.4 **
Hematocrit (%)	45.8 \pm 0.5	45.4 \pm 0.9	45.7 \pm 0.8	45.5 \pm 1.1	45.2 \pm 0.9	44.5 \pm 1.0 **
MCV (fL)	47.7 \pm 0.5	47.4 \pm 0.5	47.3 \pm 0.5	47.5 \pm 0.8	47.6 \pm 0.4	48.6 \pm 0.6 **
Reticulocyte (%)	1.7 \pm 0.2	1.8 \pm 0.4	1.8 \pm 0.2	1.7 \pm 0.2	1.9 \pm 0.2	2.8 \pm 0.3 **

Mean \pm S.D.
^{*)} Significant difference, $p < 0.05$ (Test of Dunnett)
^{**)} Significant difference, $p < 0.01$ (Test of Dunnett)

TABLE 6 HEMATOLOGY OF FEMALE RATS IN THE 13-WEEK INHALATION STUDY OF PROPIONONITRILE

Group Name	Control	6 ppm	12 ppm	25 ppm	50 ppm	100 ppm
No. of examined animals	10	10	10	9	10	10
Red blood cell ($10^6/\mu\text{L}$)	8.89 \pm 0.15	8.86 \pm 0.19	8.76 \pm 0.27	8.83 \pm 0.29	8.83 \pm 0.17	8.43 \pm 0.26 **
Hemoglobin (g/dL)	16.1 \pm 0.2	16.1 \pm 0.3	16.0 \pm 0.3	16.1 \pm 0.5	16.1 \pm 0.4	15.4 \pm 0.3 **
MCV (fL)	49.9 \pm 0.6	50.0 \pm 0.7	49.9 \pm 0.3	49.9 \pm 0.5	50.1 \pm 0.5	51.2 \pm 0.7 **
MCHC (g/dL)	36.4 \pm 0.3	36.4 \pm 0.5	36.5 \pm 0.4	36.5 \pm 0.4	36.4 \pm 0.3	35.8 \pm 0.4 **
Reticulocyte (%)	1.7 \pm 0.1	1.6 \pm 0.2	1.8 \pm 0.4	1.9 \pm 0.4	2.0 \pm 0.3	2.9 \pm 0.4 **

Mean \pm S.D.
^{*)} Significant difference, $p < 0.05$ (Test of Dunnett)
^{**)} Significant difference, $p < 0.01$ (Test of Dunnett)

TABLE 7 BIOCHEMISTRY OF MALE RATS IN THE 13-WEEK INHALATION STUDY OF PROPIONONITRILE

Group Name	Control	6 ppm	12 ppm	25 ppm	50 ppm	100 ppm
No. of examined animals	10	10	10	10	10	10
Albumin (g/dL)	3.5 ± 0.1	3.6 ± 0.1	3.6 ± 0.1	3.5 ± 0.1	3.6 ± 0.1	3.7 ± 0.1 **
T-cholesterol (mg/dL)	56 ± 6	59 ± 6	54 ± 6	57 ± 5	61 ± 2	63 ± 7 *
ALP (IU/L)	267 ± 29	268 ± 21	269 ± 21	265 ± 31	254 ± 23	224 ± 26 **

Mean ± S.D.

^{*)} Significant difference, p<0.05 (Test of Dunnett)

^{**)} Significant difference, p<0.01 (Test of Dunnett)

TABLE 8 ORGAN WEIGHTS OF MALE RATS IN THE 13-WEEK INHALATION STUDY OF PROPIONONITRILE

Group Name	Control	6 ppm	12 ppm	25 ppm	50 ppm	100 ppm	
No. of examined animals	10	10	10	10	10	10	
Body weight (g)	281 ± 16	279 ± 12	273 ± 14	280 ± 18	285 ± 17	256 ± 17	**
Testes (g)	3.025 ± 0.140	2.998 ± 0.065	3.005 ± 0.109	3.013 ± 0.171	3.013 ± 0.168	2.918 ± 0.159	
Testes (%)	1.078 ± 0.056	1.075 ± 0.059	1.103 ± 0.055	1.078 ± 0.052	1.056 ± 0.032	1.141 ± 0.055	*
Heart (g)	0.919 ± 0.056	0.923 ± 0.047	0.901 ± 0.058	0.906 ± 0.048	0.905 ± 0.049	0.892 ± 0.054	
Heart (%)	0.327 ± 0.014	0.331 ± 0.012	0.330 ± 0.011	0.324 ± 0.012	0.318 ± 0.011	0.349 ± 0.021	**
Lungs (g)	0.971 ± 0.055	0.959 ± 0.037	0.946 ± 0.046	0.983 ± 0.043	0.972 ± 0.068	0.937 ± 0.045	
Lungs (%)	0.346 ± 0.008	0.343 ± 0.013	0.347 ± 0.011	0.352 ± 0.016	0.341 ± 0.009	0.366 ± 0.014	**
Spleen (g)	0.516 ± 0.029	0.521 ± 0.034	0.510 ± 0.024	0.525 ± 0.035	0.536 ± 0.038	0.543 ± 0.041	
Spleen (%)	0.184 ± 0.007	0.187 ± 0.012	0.187 ± 0.007	0.188 ± 0.009	0.188 ± 0.008	0.212 ± 0.007	**
Liver (g)	7.047 ± 0.451	7.091 ± 0.423	6.834 ± 0.478	7.018 ± 0.621	7.364 ± 0.478	7.058 ± 0.701	
Liver (%)	2.506 ± 0.047	2.538 ± 0.114	2.504 ± 0.085	2.505 ± 0.084	2.581 ± 0.085	2.750 ± 0.128	**
Brain (g)	1.876 ± 0.072	1.879 ± 0.069	1.869 ± 0.043	1.862 ± 0.043	1.859 ± 0.037	1.852 ± 0.037	
Brain (%)	0.669 ± 0.034	0.673 ± 0.018	0.686 ± 0.031	0.668 ± 0.042	0.653 ± 0.032	0.725 ± 0.048	**

Mean ± S.D.

*) Significant difference, p<0.05 (Test of Dunnett)

**) Significant difference, p<0.01 (Test of Dunnett)

TABLE 9 ORGAN WEIGHTS OF FEMALE RATS IN THE 13-WEEK INHALATION STUDY OF PROPIONONITRILE

Group Name	Control	6 ppm	12 ppm	25 ppm	50 ppm	100 ppm	
No. of examined animals	10	10	10	10	10	10	
Body weight (g)	151 ± 6	155 ± 6	151 ± 6	154 ± 8	152 ± 10	150 ± 4	
Spleen (g)	0.344 ± 0.024	0.346 ± 0.020	0.353 ± 0.025	0.341 ± 0.018	0.355 ± 0.013	0.366 ± 0.014	
Spleen (%)	0.228 ± 0.012	0.223 ± 0.011	0.234 ± 0.016	0.222 ± 0.007	0.235 ± 0.015	0.244 ± 0.008	*
Liver (g)	3.645 ± 0.170	3.843 ± 0.172	3.701 ± 0.174	3.774 ± 0.215	3.775 ± 0.279	3.849 ± 0.139	
Liver (%)	2.420 ± 0.078	2.483 ± 0.054	2.447 ± 0.087	2.455 ± 0.084	2.491 ± 0.042	2.571 ± 0.082	**

Mean ± S.D.

*) Significant difference, p<0.05 (Test of Dunnett)

**) Significant difference, p<0.01 (Test of Dunnett)