

プロピオノニトリルのラットを用いた  
吸入による2週間毒性試験報告書

試験番号：0446

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TABLE 1  
SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE RATS IN THE 2-WEEK INHALATION STUDY OF PROPIONONITRILE

Week-Day on Study	0ppm		25ppm			50ppm			100ppm			200ppm			400ppm		
	Av.Wt. < 5>	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.
0-0	119 ( 5)	5/ 5	119 ( 5)	100	5/ 5	119 ( 5)	100	5/ 5	120 ( 5)	101	5/ 5	120 ( 5)	101	5/ 5	119 ( 5)	100	5/ 5
1-2	128 ( 5)	5/ 5	128 ( 5)	100	5/ 5	129 ( 5)	101	5/ 5	120 ( 5)	94	5/ 5	- ( -)	-	0/ 5	- ( -)	-	0/ 5
1-4	132 ( 5)	5/ 5	132 ( 5)	100	5/ 5	134 ( 5)	102	5/ 5	122 ( 5)	92	5/ 5	- ( -)	-	0/ 5	- ( -)	-	0/ 5
1-7	142 ( 5)	5/ 5	141 ( 5)	99	5/ 5	143 ( 5)	101	5/ 5	133 ( 5)	94	5/ 5	- ( -)	-	0/ 5	- ( -)	-	0/ 5
2-3	151 ( 5)	5/ 5	148 ( 5)	98	5/ 5	153 ( 5)	101	5/ 5	139 ( 5)	92	5/ 5	- ( -)	-	0/ 5	- ( -)	-	0/ 5
2-7	167 ( 5)	5/ 5	162 ( 5)	97	5/ 5	167 ( 5)	100	5/ 5	154 ( 5)	92	5/ 5	- ( -)	-	0/ 5	- ( -)	-	0/ 5

< > : 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 2-WEEK INHALATION STUDY OF PROPIONONITRILE

Week-Day on Study	0ppm		25ppm			50ppm			100ppm			200ppm			400ppm		
	Av.Wt. < 5>	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.
0-0	95 ( 5)	5/ 5	95 ( 5)	100	5/ 5	95 ( 5)	100	5/ 5	95 ( 5)	100	5/ 5	94 ( 5)	99	5/ 5	95 ( 5)	100	5/ 5
1-2	100 ( 5)	5/ 5	101 ( 5)	101	5/ 5	100 ( 5)	100	5/ 5	97 ( 5)	97	5/ 5	96 ( 5)	96	5/ 5	84 ( 3)	84	3/ 5
1-4	102 ( 5)	5/ 5	101 ( 5)	99	5/ 5	101 ( 5)	99	5/ 5	98 ( 5)	96	5/ 5	97 ( 5)	95	5/ 5	84 ( 3)	82	3/ 5
1-7	107 ( 5)	5/ 5	108 ( 5)	101	5/ 5	107 ( 5)	100	5/ 5	103 ( 5)	96	5/ 5	104 ( 5)	97	5/ 5	84 ( 3)	79	3/ 5
2-3	112 ( 5)	5/ 5	109 ( 5)	97	5/ 5	110 ( 5)	98	5/ 5	107 ( 5)	96	5/ 5	107 ( 5)	96	5/ 5	98 ( 2)	88	2/ 5
2-7	118 ( 5)	5/ 5	116 ( 5)	98	5/ 5	115 ( 5)	97	5/ 5	114 ( 5)	97	5/ 5	116 ( 5)	98	5/ 5	111 ( 2)	94	2/ 5

< > : 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 2-WEEK INHALATION STUDY OF PROPIONONITRILE

Week-Day on Study	0ppm		25ppm			50ppm			100ppm			200ppm			400ppm		
	Av.Fc. < 5>	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.
1-7	14.4 ( 5)	5/ 5	14.3 ( 5)	99	5/ 5	14.9 ( 5)	103	5/ 5	11.3 ( 5)	78	5/ 5	- ( -)	-	0/ 5	- ( -)	-	0/ 5
2-7	14.1 ( 5)	5/ 5	14.0 ( 5)	99	5/ 5	14.1 ( 5)	100	5/ 5	12.9 ( 5)	91	5/ 5	- ( -)	-	0/ 5	- ( -)	-	0/ 5

< > : 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 2-WEEK INHALATION STUDY OF PROPIONONITRILE

Week-Day on Study	0ppm		25ppm			50ppm			100ppm			200ppm			400ppm		
	Av.Fc. < 5>	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.
1-7	11.2 ( 5)	5/ 5	11.3 ( 5)	101	5/ 5	11.4 ( 5)	102	5/ 5	9.5 ( 5)	85	5/ 5	9.4 ( 5)	84	5/ 5	5.7 ( 3)	51	3/ 5
2-7	10.4 ( 5)	5/ 5	10.2 ( 5)	98	5/ 5	10.2 ( 5)	98	5/ 5	10.1 ( 5)	97	5/ 5	9.9 ( 5)	95	5/ 5	9.5 ( 2)	91	2/ 5

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

TABLE 5 HEMATOLOGY OF MALE RATS IN THE 2-WEEK INHALATION STUDY OF PROPIONONITRILE

Group Name	Control	25 ppm	50 ppm	100 ppm	200 ppm	400 ppm
No. of examined animals	5	5	5	5	0	0
MCH (pg)	19.1 ± 0.3	18.8 ± 0.2 *	18.9 ± 0.1	18.7 ± 0.2 **	—	—

Mean ± S.D.  
<sup>\*)</sup> Significant difference, p<0.05 (Test of Dunnett)  
<sup>\*\*)</sup> Significant difference, p<0.01 (Test of Dunnett)

TABLE 6 HEMATOLOGY OF FEMALE RATS IN THE 2-WEEK INHALATION STUDY OF PROPIONONITRILE

Group Name	Control	25 ppm	50 ppm	100 ppm	200 ppm	400 ppm
No. of examined animals	4	5	5	5	5	2
Red blood cell ( $10^6/\mu\text{L}$ )	8.67 ± 0.08	8.89 ± 0.12	8.87 ± 0.30	8.64 ± 0.24	8.47 ± 0.23	7.33 ?
Hemoglobin (g/dL)	16.7 ± 0.2	17.1 ± 0.3	17.0 ± 0.5	16.3 ± 0.4	16.2 ± 0.3	14.0 ?
Hematocrit (%)	44.4 ± 0.5	45.5 ± 0.8	45.4 ± 1.5	43.4 ± 0.9	43.0 ± 0.6	38.4 ?
MCH (pg)	19.2 ± 0.1	19.3 ± 0.2	19.1 ± 0.1	18.9 ± 0.2 *	19.1 ± 0.2	19.0 ?
Platelet ( $10^3/\mu\text{L}$ )	859 ± 70	808 ± 41	809 ± 55	908 ± 85	984 ± 52 *	1021 ?
Reticulocyte (%)	1.4 ± 0.2	1.2 ± 0.1	1.3 ± 0.1	2.1 ± 0.2 **	2.7 ± 0.3 **	6.2 ?
Prothrombin time (sec)	14.3 ± 1.0	14.1 ± 0.6	14.7 ± 0.8	14.8 ± 1.1	14.5 ± 0.4	16.9 ?
APTT (sec)	17.8 ± 1.9	18.0 ± 0.7	18.7 ± 0.9	18.7 ± 1.0	17.3 ± 2.1	21.7 ?
Differential WBC N-SEG (%)	17 ± 2	12 ± 1	15 ± 5	16 ± 3	17 ± 2	34 ?
LYMPHO (%)	79 ± 2	83 ± 3	81 ± 6	80 ± 4	78 ± 3	59 ?

Mean ± S.D.  
<sup>\*)</sup> Significant difference, p<0.05 (Test of Dunnett)  
<sup>\*\*)</sup> Significant difference, p<0.01 (Test of Dunnett)  
<sup>?)</sup> The test of Dunnett could not be applied because number of data was less than three.

TABLE 7 BIOCHEMISTRY OF FEMALE RATS IN THE 2-WEEK INHALATION STUDY OF PROPIONONITRILE

Group Name	Control	25 ppm	50 ppm	100 ppm	200 ppm	400 ppm
No. of examined animals	4	5	5	5	5	2
Glucose (mg/dL)	128 ± 7	131 ± 7	120 ± 12	121 ± 16	126 ± 12	158 ?
ALP (IU/L)	566 ± 46	562 ± 16	578 ± 10	489 ± 43	484 ± 45 *	583 ?
Urea Nitrogen (mg/dL)	17.7 ± 1.0	18.4 ± 0.7	17.2 ± 1.2	15.6 ± 0.7 *	16.1 ± 1.5	15.2 ?

Mean ± S.D.

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

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

?) The test of Dunnett could not be applied because number of data was less than three.

TABLE 8 ORGAN WEIGHTS OF MALE RATS IN THE 2-WEEK INHALATION STUDY OF PROPIONONITRILE

Group Name	Control	25 ppm	50 ppm	100 ppm	200 ppm	400 ppm
No. of examined animals	5	5	5	5	0	0
Body weight (g)	148 ± 8	145 ± 9	149 ± 3	138 ± 8	—	—
Thymus (g)	0.277 ± 0.027	0.285 ± 0.029	0.274 ± 0.022	0.233 ± 0.022 *	—	—
Thymus (%)	0.187 ± 0.010	0.196 ± 0.015	0.185 ± 0.017	0.169 ± 0.016	—	—
Spleen (g)	0.362 ± 0.014	0.331 ± 0.033	0.343 ± 0.014	0.318 ± 0.021 *	—	—
Spleen (%)	0.245 ± 0.007	0.227 ± 0.011 *	0.231 ± 0.010	0.231 ± 0.010	—	—

Mean ± S.D.  
<sup>\*)</sup> Significant difference, p<0.05 (Test of Dunnett)  
<sup>\*\*)</sup> Significant difference, p<0.01 (Test of Dunnett)

TABLE 9 ORGAN WEIGHTS OF FEMALE RATS IN THE 2-WEEK INHALATION STUDY OF PROPIONONITRILE

Group Name	Control	25 ppm	50 ppm	100 ppm	200 ppm	400 ppm
No. of examined animals	5	5	5	5	5	2
Body weight (g)	105 ± 3	103 ± 3	103 ± 4	103 ± 3	103 ± 3	94 ?
Thymus (g)	0.229 ± 0.015	0.241 ± 0.015	0.237 ± 0.011	0.221 ± 0.012	0.211 ± 0.010	0.113 ?
Thymus (%)	0.218 ± 0.013	0.234 ± 0.015	0.230 ± 0.009	0.215 ± 0.007	0.204 ± 0.012	0.121 ?
Adrenals (g)	0.042 ± 0.005	0.041 ± 0.003	0.042 ± 0.001	0.042 ± 0.005	0.046 ± 0.002	0.048 ?
Adrenals (%)	0.040 ± 0.005	0.040 ± 0.003	0.040 ± 0.001	0.041 ± 0.004	0.045 ± 0.002	0.051 ?
Ovaries (g)	0.065 ± 0.012	0.060 ± 0.011	0.068 ± 0.014	0.068 ± 0.009	0.070 ± 0.009	0.054 ?
Ovaries (%)	0.062 ± 0.010	0.058 ± 0.011	0.066 ± 0.011	0.067 ± 0.011	0.068 ± 0.009	0.058 ?
Heart (g)	0.466 ± 0.039	0.461 ± 0.031	0.457 ± 0.023	0.498 ± 0.051	0.523 ± 0.035	0.536 ?
Heart (%)	0.442 ± 0.030	0.447 ± 0.032	0.444 ± 0.024	0.485 ± 0.042	0.505 ± 0.025 *	0.573 ?
Spleen (g)	0.263 ± 0.014	0.240 ± 0.014	0.257 ± 0.032	0.245 ± 0.018	0.251 ± 0.022	0.216 ?
Spleen (%)	0.251 ± 0.011	0.233 ± 0.014	0.249 ± 0.027	0.239 ± 0.011	0.243 ± 0.016	0.231 ?
Liver (g)	3.546 ± 0.262	3.158 ± 0.105 *	3.236 ± 0.225	3.343 ± 0.208	3.568 ± 0.219	4.128 ?
Liver (%)	3.379 ± 0.352	3.066 ± 0.040	3.140 ± 0.136	3.257 ± 0.126	3.449 ± 0.116	4.414 ?
Brain (g)	1.654 ± 0.018	1.620 ± 0.013	1.591 ± 0.009 **	1.617 ± 0.023	1.609 ± 0.037 *	1.602 ?
Brain (%)	1.574 ± 0.052	1.574 ± 0.039	1.546 ± 0.055	1.577 ± 0.028	1.557 ± 0.063	1.714 ?

Mean ± S.D.  
<sup>\*)</sup> Significant difference, p<0.05 (Test of Dunnett)  
<sup>\*\*)</sup> Significant difference, p<0.01 (Test of Dunnett)  
<sup>?)</sup> The test of Dunnett could not be applied because number of data was less than three.

TABLE 10 INCIDENCES OF SELECTED LESIONS OF MALE RATS IN THE 2-WEEK  
 INHALATION STUDY OF PROPIONONITRILE  
 (DEAD AND MORIBUND ANIMALS)

Group		200 ppm	400 ppm
Number of examined animals		5	5
Organ Findings	Grade		
Nasal cavity Congestion	1+	5	5
Lung Congestion	1+	3	3
Hemorrhage	1+	1	3
Grade	1+: Slight		



TABLE 11 INCIDENCES OF SELECTED LESIONS OF FEMALE RATS IN THE 2-WEEK  
 INHALATION STUDY OF PROPIONONITRILE  
 (DEAD AND MORIBUND ANIMALS)

Group		400 ppm
Number of examined animals		3
Organ	Grade	
Findings		
Nasal cavity		
Congestion	1+	2
Lung		
Congestion	1+	3
Thymus		
Atrophy	1+	1
Adrenal		
Hemorrhage	1+	1
Grade	1+: Slight	