酸化チタン（ナノ粒子、アナターゼ型）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：0863

APPENDICES

APPENDICES

APPENDIX 1

AEROSOL PARTICLE SIZE DISTRIBUTION ANALYSIS

AEROSOL PARTICLE SIZE DISTRIBUTION ANALYSIS

1-WEEK ON ADMINISTRATION

Stage No. (μm)		6.5 mg/m^3 Flow：10 ℓ/min Time：16min			12.5 mg/m^3 Flow：10 ℓ/min Time：8min			25 mg/m^3 Flow：10 ℓ/min Time：4min			50 mg/m^3 Flow：10 ℓ/min Time：2min		
		Weight (mg)	Mass Fraction (%)	Cumulative Rate (%)	Weight (mg)	Mass Fraction (%)	Cumulative Rate (%)	Weight (mg)	Mass Fraction (%)	Cumulative Rate (%)	Weight (mg)	Mass Fraction (%)	Cumulative Rate (%)
1	10	0.007	1.12	100.00	0.004	0.55	100.00	0.006	0.84	100.00	0.009	1.23	100.00
2	5.6	0.010	1.59	98.88	0.011	1.50	99.45	0.016	2.24	99.16	0.034	4.66	98.77
3	3.2	0.053	8.45	97.29	0.073	9.96	97.95	0.075	10.52	96.91	0.062	8.49	94.11
4	1.8	0.187	29.82	88.84	0.194	26.47	87.99	0.206	28.89	86.40	0.245	33.56	85.62
5	1.0	0.255	40.67	59.01	0.288	39.29	61.53	0.273	38.29	57.50	0.273	37.40	52.05
6	0.56	0.091	14.51	18.34	0.136	18.55	22.24	0.103	14.45	19.21	0.081	11.10	14.66
7	0.32	0.018	2.87	3.83	0.019	2.59	3.68	0.027	3.79	4.77	0.018	2.47	3.56
8	0.18	0.004	0.64	0.96	0.005	0.68	1.09	0.004	0.56	0.98	0.005	0.68	1.10
9	0.10	0.002	0.32	0.32	0.003	0.41	0.41	0.003	0.42	0.42	0.003	0.41	0.41
10	0.056	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00
11	0.032	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00
12	0.018	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00
13	0.010	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00
Final	～0.010	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00
Total		0.627	100	-	0.733	100	-	0.713	100	-	0.730	100	-

AEROSOL PARTICLE SIZE DISTRIBUTION ANALYSIS(CONTINUED)

6-WEEK ON ADMINISTRATION

Stage No. (μm)		6.5 mg/m^3 Flow：10 ℓ/min Time：16min			12.5 mg/m^3 Flow：10 ℓ/min Time：8min			25 mg/m^3 Flow：10 ℓ/min Time：4min			50 mg/m^3 Flow：10 ℓ/min Time：2min		
		Weight (mg)	Mass Fraction (%)	Cumulative Rate (%)	Weight (mg)	Mass Fraction (%)	Cumulative Rate (%)	Weight (mg)	Mass Fraction (%)	Cumulative Rate (%)	Weight (mg)	Mass Fraction (%)	Cumulative Rate (%)
1	10	0.004	0.53	100.00	0.004	0.55	100.00	0.006	0.79	100.00	0.004	0.63	100.00
2	5.6	0.009	1.20	99.47	0.009	1.25	99.45	0.009	1.19	99.21	0.010	1.58	99.37
3	3.2	0.083	11.02	98.27	0.058	8.03	98.20	0.085	11.26	98.01	0.069	10.94	97.78
4	1.8	0.219	29.08	87.25	0.175	24.24	90.17	0.237	31.39	86.75	0.191	30.27	86.85
5	1.0	0.313	41.57	58.17	0.303	41.97	65.93	0.286	37.88	55.36	0.250	39.62	56.58
6	0.56	0.102	13.55	16.60	0.144	19.94	23.96	0.103	13.64	17.48	0.090	14.26	16.96
7	0.32	0.019	2.52	3.05	0.021	2.91	4.02	0.023	3.05	3.84	0.012	1.90	2.69
8	0.18	0.003	0.40	0.53	0.006	0.83	1.11	0.004	0.53	0.79	0.004	0.63	0.79
9	0.10	0.001	0.13	0.13	0.002	0.28	0.28	0.002	0.26	0.26	0.001	0.16	0.16
10	0.056	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00
11	0.032	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00
12	0.018	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00
13	0.010	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00
Final	～0.010	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00
Total		0.753	100	-	0.722	100	-	0.755	100	-	0.631	100	-

AEROSOL PARTICLE SIZE DISTRIBUTION ANALYSIS(CONTINUED)

13-WEEK ON ADMINISTRATION

Stage No. (μm)		6.5 mg/m^3 Flow：10 ℓ/min Time：16min			12.5 mg/m^3 Flow：10 ℓ/min Time：8min			25 mg/m^3 Flow：10 ℓ/min Time：4min			50 mg/m^3 Flow：10 ℓ/min Time：2min		
		Weight (mg)	Mass Fraction (%)	Cumulative Rate (%)	Weight (mg)	Mass Fraction (%)	Cumulative Rate (%)	Weight (mg)	Mass Fraction (%)	Cumulative Rate (%)	Weight (mg)	Mass Fraction (%)	Cumulative Rate (%)
1	10	0.004	0.61	100.00	0.003	0.47	100.00	0.004	0.41	100.00	0.007	1.02	100.00
2	5.6	0.007	1.07	99.39	0.009	1.40	99.53	0.019	1.94	99.59	0.013	1.90	98.98
3	3.2	0.065	9.97	98.31	0.078	12.15	98.13	0.123	12.54	97.66	0.079	11.55	97.08
4	1.8	0.201	30.83	88.34	0.197	30.69	85.98	0.320	32.62	85.12	0.212	30.99	85.53
5	1.0	0.260	39.88	57.52	0.252	39.25	55.30	0.378	38.53	52.50	0.262	38.30	54.53
6	0.56	0.083	12.73	17.64	0.086	13.40	16.04	0.114	11.62	13.97	0.089	13.01	16.23
7	0.32	0.024	3.68	4.91	0.011	1.71	2.65	0.016	1.63	2.34	0.015	2.19	3.22
8	0.18	0.005	0.77	1.23	0.004	0.62	0.93	0.004	0.41	0.71	0.004	0.58	1.02
9	0.10	0.003	0.46	0.46	0.002	0.31	0.31	0.003	0.31	0.31	0.003	0.44	0.44
10	0.056	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00
11	0.032	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00
12	0.018	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00
13	0.010	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00
Final	～0.010	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00	0.000	0.00	0.00
Total		0.652	100	-	0.642	100	-	0.981	100	-	0.684	100	-

APPENDIX 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-WEEK INHALATION STUDY OF TITANIUM DIOXIDE

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER
IN THE 13-WEEK INHALATION STUDY OF TITANIUM DIOXIDE

Group Name	Temperature (℃) Mean ± S.D.	Humidity (%) Mean ± S.D.	Ventilation Rate (L/min) Mean ± S.D.	Air Change (time/h) Mean
Control	22.6 ± 0.3	58.0 ± 0.9	206.0 ± 2.5	10.0
6.3 mg/m^3	22.8 ± 0.5	54.7 ± 4.1	208.2 ± 2.9	10.1
12.5 mg/m^3	22.7 ± 0.4	52.3 ± 3.3	209.8 ± 2.7	10.2
25 mg/m^3	22.8 ± 0.4	52.9 ± 3.1	210.5 ± 2.9	10.2
50 mg/m^3	22.9 ± 0.5	54.3 ± 2.8	209.0 ± 3.3	10.1

APPENDIX 3

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK INHALATION STUDY OF TITANIUM DIOXIDE

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK INHALATION STUDY OF TITANIUM DIOXIDE

Item	Method	Unit	Decimal place
Hematology			
Red blood cell (RBC)	Light scattering method [1]	$\times 10^6/\mu$ L	2
Hemoglobin(Hgb)	Cyanmethemoglobin method [1]	g/dL	1
Hematocrit(Hct)	Calculated as RBC×MCV/10 [1]	%	1
Mean corpuscular volume(MCV)	Light scattering method [1]	fL	1
Mean corpuscular hemoglobin(MCH)	Calculated as Hgb/RBC×10 [1]	pg	1
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as Hgb/Hct×100 [1]	g/dL	1
Platelet	Light scattering method [1]	$\times 10^3/\mu$ L	0
Reticulocyte	Light scattering method [1]	%	1
Prothrombin time	Quick one stage method [2]	sec	1
Activated partial thromboplastin time(APTT)	Ellagic acid activated method [2]	sec	1
White blood cell(WBC)	Light scattering method [1]	$\times 10^3/\mu$ L	2
Differential WBC	Light scattering method [1]	%	1
Biochemistry			
Total protein(TP)	Biuret method [3]	g/dL	1
Albumin (Alb)	BCG method [3]	g/dL	1
A/G ratio	Calculated as Alb/(TP－Alb) [3]	－	1
T-bilirubin	BOD method [3]	mg/dL	2
Glucose	GlcK･G-6-PDH method [3]	mg/dL	0
T-cholesterol	CE･COD･POD method [3]	mg/dL	0
Triglyceride	MGLP･GK･GPO･POD method [3]	mg/dL	0
Phospholipid	PLD･ChOD･POD method [3]	mg/dL	0
Aspartate aminotransferase (AST)	JSCC method [3]	U/L	0
Alanine aminotransferase (ALT)	JSCC method [3]	U/L	0
Lactate dehydrogenase (LDH)	JSCC method [3]	U/L	0
Alkaline phosphatase (ALP)	JSCC method [3]	U/L	0
γ -Glutamyl transpeptidase (γ -GTP)	JSCC method [3]	U/L	1
Creatine kinase (CK)	JSCC method [3]	U/L	0
Urea nitrogen	Urease･GLDH method [3]	mg/dL	1
Creatinine	Creatinase･SOD･POD method [3]	mg/dL	2
Sodium	Ion selective electrode method [3]	mEq/L	0
Potassium	Ion selective electrode method [3]	mEq/L	1
Chloride	Ion selective electrode method [3]	mEq/L	0
Calcium	OCPC method [3]	mg/dL	1
Inorganic phosphorus	PNP･XOD･POD method [3]	mg/dL	1

1) Automatic blood cell analyzer (ADVIA120 : Siemens Healthcare Diagnostics Inc.)
2) Automatic coagulometer (Sysmex CA-510 : Sysmex Corporation)
3) Automatic analyzer (Hitachi 7080 : Hitachi,Ltd.)

APPENDIX 4

METHODS, UNITS AND DECIMAL PLACE FOR CYTOLOGY AND BIOCHEMISTRY OF BALF

METHODS, UNITS AND DECIMAL PLACE FOR CYTOLOGY AND BIOCHEMISTRY OF BALF

	Method	Unit	Decimal place
Cytology			
Total cell count	Flow Cytometry method [1)]	$\times 10^3/\mu L$	2
Differential	Visual observation method (May-Grunwald-Giemsa stain)	%	1
Biochemistry			
Total protein(TP)	Pyrogallol red method [2)]	μ g/mL	0
Albumin (Alb)	Immuno-nephelometry [2)]	μ g/ mL	0
LDH	JSCC method [2)]	U/L	0
ALP	JSCC method [2)]	U/L	0
γ -GTP	JSCC method [2)]	U/L	1

1) Automatic blood cell analyzer (ADVIA120 : Siemens Healthcare Diagnostics Inc.)
2) Automatic analyzer (Hitachi 7080 : Hitachi,Ltd.)