

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 2 週間毒性試験報告書

試験番号：0856

TABLES

TABLES

TABLE A	CONCENTRATIONS OF TITANIUM DIOXIDE IN THE INHALATION CHAMBER OF THE 2-WEEK INHALATION STUDY
TABLE B1	SURVIVAL ANIMAL NUMBERS: MALE
TABLE B2	SURVIVAL ANIMAL NUMBERS: FEMALE
TABLE C1	CLINICAL OBSERVATION: MALE
TABLE C2	CLINICAL OBSERVATION: FEMALE
TABLE D1	BODY WEIGHT CHANGES AND SURVIVAL ANIMAL NUMBERS : MALE
TABLE D2	BODY WEIGHT CHANGES AND SURVIVAL ANIMAL NUMBERS : FEMALE
TABLE D3	BODY WEIGHT CHANGES: MALE
TABLE D4	BODY WEIGHT CHANGES: FEMALE
TABLE E1	FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS: MALE
TABLE E2	FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS: FEMALE
TABLE E3	FOOD CONSUMPTION CHANGES: MALE
TABLE E4	FOOD CONSUMPTION CHANGES: FEMALE
TABLE F1	HEMATOLOGY: MALE
TABLE F2	HEMATOLOGY: FEMALE
TABLE G1	BIOCHEMISTRY: MALE
TABLE G2	BIOCHEMISTRY: FEMALE

TABLES (CONTINUED)

TABLE	H1	BALF: CYTOLOGICAL ANALYSIS: MALE
TABLE	H2	BALF: CYTOLOGICAL ANALYSIS: FEMALE
TABLE	I1	BALF: BIOCHEMICAL ANALYSIS: MALE
TABLE	I2	BALF: BIOCHEMICAL ANALYSIS: FEMALE
TABLE	J1	ORGAN WEIGHT, ABSOLUTE: MALE
TABLE	J2	ORGAN WEIGHT, ABSOLUTE: FEMALE
TABLE	K1	ORGAN WEIGHT, RELATIVE: MALE
TABLE	K2	ORGAN WEIGHT, RELATIVE: FEMALE
TABLE	L1	HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS : MALE
TABLE	L2	HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS : FEMALE
TABLE	M	AMOUNT OF TITANIUM DIOXIDE IN LUNGS

TABLE A

CONCENTRATIONS OF TITANIUM DIOXIDE
IN THE INHALATION CHAMBER
OF THE 2-WEEK INHALATION STUDY

CONCENTRATIONS OF TITANIUM DIOXIDE IN THE INHALATION
CHAMBER OF THE 2-WEEK INHALATION STUDY

Group Name	Concentration(mg/m ³) Mean ± S.D.
Control	0.000 ± 0.000
0.2 mg/m ³	0.204 ± 0.011
1 mg/m ³	1.013 ± 0.034
5 mg/m ³	5.091 ± 0.575
25 mg/m ³	24.541 ± 1.480

TABLE B1

SURVIVAL ANIMAL NUMBERS : MALE

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCrI CrIj[F344/DuCrj]
 REPORT TYPE : A1 2
 SEX : MALE

SURVIVAL ANIMAL NUMBERS

Group Name	Animals At start	Administration (Days)													
		0-0	1-1	1-2	1-3	1-4	1-5	1-6	1-7	2-1	2-2	2-3	2-4	2-5	2-6
Control	5	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0
0.2 mg/m3	5	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0
1 mg/m3	5	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0
5 mg/m3	5	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0
25 mg/m3	5	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0
		Number of survival/ Number of effective animals Survival rate(%)													

STUDY NO. : 0856
ANIMAL : RAT F344/DuCrI CrIj[F344/DuCrj]
REPORT TYPE : A1 2
SEX : MALE

SURVIVAL ANIMAL NUMBERS

Group Name	Animals At start	Administration (Days) 2-7
Control	5	5/ 5 100.0
0.2 mg/m3	5	5/ 5 100.0
1 mg/m3	5	5/ 5 100.0
5 mg/m3	5	5/ 5 100.0
25 mg/m3	5	5/ 5 100.0

Number of survival/ Number of effective animals
Survival rate(%)

TABLE B2

SURVIVAL ANIMAL NUMBERS : FEMALE

STUDY NO. : 0856

SURVIVAL ANIMAL NUMBERS

ANIMAL : RAT F344/DuCrI CrIj[F344/DuCrj]

REPORT TYPE : A1 2

SEX : FEMALE

Group Name	Animals At start	Administration (Days)													
		0-0	1-1	1-2	1-3	1-4	1-5	1-6	1-7	2-1	2-2	2-3	2-4	2-5	2-6
Control	5	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0
0.2 mg/m3	5	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0
1 mg/m3	5	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0
5 mg/m3	5	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0
25 mg/m3	5	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0	5/ 5 100.0
		Number of survival/ Number of effective animals Survival rate(%)													

STUDY NO. : 0856

SURVIVAL ANIMAL NUMBERS

ANIMAL : RAT F344/DuCrI CrIj[F344/DuCrj]

REPORT TYPE : A1 2

SEX : FEMALE

Group Name	Animals At start	Administration (Days) 2-7
Control	5	5/ 5 100.0
0.2 mg/m3	5	5/ 5 100.0
1 mg/m3	5	5/ 5 100.0
5 mg/m3	5	5/ 5 100.0
25 mg/m3	5	5/ 5 100.0

Number of survival/ Number of effective animals
Survival rate(%)

TABLE C1

CLINICAL OBSERVATION : MALE

STUDY NO. : 0856
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 1

Clinical sign	Group Name	Administration Week-day	
		1-7	2-7
NON REMARKABLE	Control	5	5
	0.2 mg/m3	5	5
	1 mg/m3	5	5
	5 mg/m3	5	5
	25 mg/m3	5	5

(HAN190)

BAIS 5

TABLE C2

CLINICAL OBSERVATION : FEMALE

STUDY NO. : 0856
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 2

Clinical sign	Group Name	Administration Week-day	
		1-7	2-7
NON REMARKABLE	Control	5	5
	0.2 mg/m3	5	5
	1 mg/m3	5	5
	5 mg/m3	5	5
	25 mg/m3	5	5

(HAN190)

BAIS 5

TABLE D1

BODY WEIGHT CHANGES AND
SURVIVAL ANIMAL NUMBERS : MALE

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 UNIT : g
 REPORT TYPE : A1 2
 SEX : MALE

MEAN BODY WEIGHTS AND SURVIVAL

Week-Day on Study	Control		0.2 mg/m3		1 mg/m3		5 mg/m3		25 mg/m3		
	Av. Wt. < 5>	No. of Surviv. < 5>	Av. Wt. < 5>	% of cont. < 5>	No. of Surviv. < 5>	Av. Wt. < 5>	% of cont. < 5>	No. of Surviv. < 5>	Av. Wt. < 5>	% of cont. < 5>	No. of Surviv. < 5>
0-0	114 (5)	5/ 5	114 (5)	100	5/ 5	114 (5)	100	5/ 5	114 (5)	100	5/ 5
1-7	141 (5)	5/ 5	140 (5)	99	5/ 5	141 (5)	100	5/ 5	139 (5)	99	5/ 5
2-7	169 (5)	5/ 5	166 (5)	98	5/ 5	167 (5)	99	5/ 5	169 (5)	100	5/ 5

< >:No. of effective animals, ():No. of measured animals Av. Wt. : g

TABLE D2

BODY WEIGHT CHANGES AND
SURVIVAL ANIMAL NUMBERS : FEMALE

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 UNIT : g
 REPORT TYPE : A1 2
 SEX : FEMALE

MEAN BODY WEIGHTS AND SURVIVAL

Week-Day on Study	Control		0.2 mg/m3		1 mg/m3		5 mg/m3		25 mg/m3					
	Av. Wt. < 5>	No. of Surviv. < 5>	Av. Wt. < 5>	% of cont. < 5>	No. of Surviv. < 5>	Av. Wt. < 5>	% of cont. < 5>	No. of Surviv. < 5>	Av. Wt. < 5>	% of cont. < 5>	No. of Surviv. < 5>			
0-0	94 (5)	5/ 5	94 (5)	100	5/ 5	94 (5)	100	5/ 5	94 (5)	100	5/ 5	94 (5)	100	5/ 5
1-7	108 (5)	5/ 5	106 (5)	98	5/ 5	105 (5)	97	5/ 5	103 (5)	95	5/ 5	102 (5)	94	5/ 5
2-7	123 (5)	5/ 5	118 (5)	96	5/ 5	119 (5)	97	5/ 5	116 (5)	94	5/ 5	114 (5)	93	5/ 5

< >:No. of effective animals, ():No. of measured animals Av. Wt. : g

TABLE D3

BODY WEIGHT CHANGES : MALE

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 UNIT : g
 REPORT TYPE : A1 2
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

Group Name	Administration week-day					
	0-0		1-7		2-7	
Control	114±	4	141±	5	169±	9
0.2 mg/m3	114±	4	140±	7	166±	9
1 mg/m3	114±	4	141±	5	167±	5
5 mg/m3	114±	4	139±	5	169±	8
25 mg/m3	114±	4	137±	5	164±	6

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

TABLE D4

BODY WEIGHT CHANGES : FEMALE

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 UNIT : g
 REPORT TYPE : A1 2
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

Group Name	Administration week-day					
	0-0		1-7		2-7	
Control	94±	3	108±	3	123±	4
0.2 mg/m3	94±	3	106±	4	118±	5
1 mg/m3	94±	3	105±	5	119±	6
5 mg/m3	94±	3	103±	1	116±	3
25 mg/m3	94±	4	102±	6	114±	7

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

TABLE E1

FOOD CONSUMPTION CHANGES AND
SURVIVAL ANIMAL NUMBERS : MALE

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 UNIT : g
 REPORT TYPE : A1 2
 SEX : MALE

MEAN FOOD CONSUMPTION(FC) AND SURVIVAL

Week-Day on Study	Control		0.2 mg/m3			1 mg/m3			5 mg/m3			25 mg/m3		
	Av. FC.	No. of Surviv. < 5>	Av. FC.	% of cont. < 5>	No. of Surviv.	Av. FC.	% of cont. < 5>	No. of Surviv.	Av. FC.	% of cont. < 5>	No. of Surviv.	Av. FC.	% of cont. < 5>	No. of Surviv.
1-7	14.9 (5)	5/ 5	15.3 (5)	103	5/ 5	16.6 (5)	111	5/ 5	15.8 (5)	106	5/ 5	15.2 (5)	102	5/ 5
2-7	16.1 (5)	5/ 5	15.8 (5)	98	5/ 5	16.3 (5)	101	5/ 5	16.1 (5)	100	5/ 5	15.3 (5)	95	5/ 5

< >:No. of effective animals, ():No. of measured animals Av. FC. : g

TABLE E2

**FOOD CONSUMPTION CHANGES AND
SURVIVAL ANIMAL NUMBERS : FEMALE**

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 UNIT : g
 REPORT TYPE : A1 2
 SEX : FEMALE

MEAN FOOD CONSUMPTION(FC) AND SURVIVAL

Week-Day on Study	Control		0.2 mg/m3			1 mg/m3			5 mg/m3			25 mg/m3		
	Av. FC.	No. of Surviv. < 5>	Av. FC.	% of cont. < 5>	No. of Surviv.	Av. FC.	% of cont. < 5>	No. of Surviv.	Av. FC.	% of cont. < 5>	No. of Surviv.	Av. FC.	% of cont. < 5>	No. of Surviv.
1-7	11.8 (5)	5/ 5	11.7 (5)	99	5/ 5	11.7 (5)	99	5/ 5	12.1 (5)	103	5/ 5	11.4 (5)	97	5/ 5
2-7	12.0 (5)	5/ 5	11.3 (5)	94	5/ 5	11.1 (5)	93	5/ 5	11.6 (5)	97	5/ 5	11.2 (5)	93	5/ 5

< >:No. of effective animals, ():No. of measured animals Av. FC. : g

TABLE E3

FOOD CONSUMPTION CHANGES : MALE

STUDY NO. : 0856
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective)	
	1-7(7)	2-7(7)
Control	14.9± 0.5	16.1± 0.8
0.2 mg/m3	15.3± 0.9	15.8± 1.6
1 mg/m3	16.6± 1.3	16.3± 0.8
5 mg/m3	15.8± 0.4	16.1± 0.8
25 mg/m3	15.2± 1.0	15.3± 0.8

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

TABLE E4

FOOD CONSUMPTION CHANGES : FEMALE

STUDY NO. : 0856
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective)	
	1-7(7)	2-7(7)
Control	11.8± 0.3	12.0± 0.6
0.2 mg/m3	11.7± 0.5	11.3± 0.6
1 mg/m3	11.7± 1.0	11.1± 0.9
5 mg/m3	12.1± 0.3	11.6± 0.3
25 mg/m3	11.4± 0.6	11.2± 0.9

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

TABLE F1

HEMATOLOGY : MALE

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 MEASURE. TIME : 1
 SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (3W)

Group Name	NO. of Animals	RED BLOOD CELL 10 ⁶ /μl		HEMOGLOBIN g/dl		HEMATOCRIT %		MCV fl		MCH pg		MCHC g/dl		PLATELET 10 ³ /μl	
Control	4	8.53±	0.21	14.9±	0.3	45.4±	0.9	53.3±	0.8	17.5±	0.3	32.9±	0.5	932±	69
0.2 mg/m3	5	8.59±	0.22	14.9±	0.3	45.4±	1.1	52.8±	0.3	17.4±	0.1	32.9±	0.1	953±	31
1 mg/m3	5	8.68±	0.15	15.0±	0.2	46.0±	0.7	53.0±	0.3	17.3±	0.2	32.7±	0.5	976±	20
5 mg/m3	5	8.71±	0.09	15.0±	0.1	46.3±	0.4	53.1±	0.4	17.3±	0.2	32.5±	0.4	988±	17
25 mg/m3	4	8.53±	0.20	14.8±	0.3	45.4±	1.4	53.2±	0.6	17.4±	0.2	32.6±	0.6	964±	29

Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01

Test of Dunnett

STUDY NO. : 0856
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (3W)

PAGE : 2

Group Name	NO. of Animals	RETICULOCYTE %	
Control	4	3.2±	0.6
0.2 mg/m3	5	2.9±	0.2
1 mg/m3	5	3.0±	0.2
5 mg/m3	5	3.2±	0.4
25 mg/m3	4	3.2±	0.3

Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 MEASURE. TIME : 1
 SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (3W)

Group Name	NO. of Animals	WBC		Differential		WBC (%)		MONO	EOSINO	BASO	OTHER		
		10 ⁹ /μl		NEUTRO		LYMPHO							
Control	4	2.67±	0.68	25±	2	72±	2	2±	0	1±	1	1±	1
0.2 mg/m3	5	3.02±	0.47	30±	5	66±	5	3±	1	1±	0	0±	1
1 mg/m3	5	2.81±	0.40	28±	5	68±	5	2±	0	1±	0	1±	1
5 mg/m3	5	2.90±	0.44	28±	4	69±	4	2±	0	1±	0	1±	1
25 mg/m3	4	3.84±	0.50*	22±	2	74±	1	2±	1	1±	0	0±	1

Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01 Test of Dunnett

TABLE F2

HEMATOLOGY : FEMALE

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 MEASURE. TIME : 1
 SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (3W)

Group Name	NO. of Animals	RED BLOOD CELL 10 ⁶ /μl		HEMOGLOBIN g/dl		HEMATOCRIT %		MCV fl		MCH pg		MCHC g/dl		PLATELET 10 ³ /μl	
Control	3	8.77±	0.26	15.2±	0.5	45.7±	1.2	52.2±	0.4	17.4±	0.2	33.3±	0.4	829±	39
0.2 mg/m3	4	8.89±	0.16	15.6±	0.4	46.1±	0.7	51.8±	0.3	17.6±	0.2	33.8±	0.4	881±	58
1 mg/m3	5	9.00±	0.17	15.8±	0.3	47.2±	0.9	52.4±	0.3	17.6±	0.1	33.5±	0.2	861±	52
5 mg/m3	4	8.96±	0.15	15.7±	0.1	46.8±	0.7	52.2±	0.2	17.5±	0.3	33.6±	0.4	838±	69
25 mg/m3	3	8.89±	0.12	15.7±	0.3	47.0±	0.7	52.9±	0.7	17.6±	0.1	33.4±	0.4	841±	48

Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01

Test of Dunnett

STUDY NO. : 0856
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (3W)

Group Name	NO. of Animals	RETICULOCYTE %	
Control	3	1.6±	0.2
0.2 mg/m3	4	1.5±	0.2
1 mg/m3	5	1.5±	0.3
5 mg/m3	4	1.4±	0.1
25 mg/m3	3	1.6±	0.2

Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 MEASURE. TIME : 1
 SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (3W)

Group Name	NO. of Animals	WBC		Differential		WBC (%)		MONO	EOSINO	BASO	OTHER		
		10 ⁹ /μl		NEUTRO		LYMPHO							
Control	3	2.09±	0.59	19±	3	76±	2	3±	1	2±	1	1±	1
0.2 mg/m3	4	2.65±	0.28	24±	8	71±	9	2±	1	2±	1	0±	1
1 mg/m3	5	2.92±	0.76	21±	5	75±	5	2±	0	1±	0	1±	1
5 mg/m3	4	3.09±	0.96	19±	5	78±	5	2±	1	1±	0	0±	1
25 mg/m3	3	3.34±	0.14	14±	3	82±	3	2±	1	1±	0	0±	0

Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01 Test of Dunnett

TABLE G1

BIOCHEMISTRY : MALE

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 MEASURE. TIME : 1
 SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (3W)

Group Name	NO. of Animals	TOTAL PROTEIN g/dl		ALBUMIN g/dl		A/G RATIO		T-BILIRUBIN mg/dl		GLUCOSE mg/dl		T-CHOLESTEROL mg/dl		TRIGLYCERIDE mg/dl	
Control	5	5.5±	0.2	3.2±	0.1	1.4±	0.0	0.02±	0.00	165±	20	66±	3	45±	14
0.2 mg/m3	5	5.6±	0.2	3.3±	0.1	1.4±	0.1	0.02±	0.00	157±	4	64±	4	39±	11
1 mg/m3	5	5.5±	0.1	3.1±	0.1	1.3±	0.1	0.02±	0.00	149±	9	60±	2	31±	2
5 mg/m3	5	5.5±	0.1	3.1±	0.1	1.3±	0.0	0.02±	0.00	170±	28	61±	1	36±	13
25 mg/m3	5	5.4±	0.1	3.1±	0.1	1.4±	0.1	0.03±	0.01	163±	24	63±	5	43±	16

Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCrI CrI j[F344/DuCrj]
 MEASURE. TIME : 1
 SEX : MALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (3W)

REPORT TYPE : A1

Group Name	NO. of Animals	PHOSPHOLIPID mg/dl		AST U/L		ALT U/L		LDH U/L		ALP U/L		G-GTP U/L		CK U/L	
Control	5	119±	4	68±	6	34±	2	133±	53	1135±	139	0.7±	0.4	270±	14
0.2 mg/m3	5	118±	5	68±	8	35±	1	68±	5	1161±	70	1.0±	0.3	256±	13
1 mg/m3	5	110±	1**	67±	3	35±	2	82±	31	1167±	118	0.6±	0.2	252±	30
5 mg/m3	5	109±	2**	65±	3	33±	2	70±	12	1182±	95	0.4±	0.3	246±	24
25 mg/m3	5	116±	6	65±	4	33±	3	73±	11	1110±	80	0.6±	0.3	243±	19

Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 MEASURE. TIME : 1
 SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (3W)

Group Name	NO. of Animals	UREA NITROGEN mg/dl		CREATININE mg/dl		SODIUM mEq/l		POTASSIUM mEq/l		CHLORIDE mEq/l		CALCIUM mg/dl		INORGANIC PHOSPHORUS mg/dl	
Control	5	18.7±	0.9	0.25±	0.01	145±	2	3.1±	0.3	104±	1	10.0±	0.2	7.9±	0.7
0.2 mg/m3	5	19.5±	2.2	0.25±	0.01	146±	1	3.3±	0.1	104±	1	10.2±	0.2	8.3±	0.4
1 mg/m3	5	17.6±	1.5	0.24±	0.01	147±	1	3.2±	0.3	105±	1	10.2±	0.2	8.6±	0.4
5 mg/m3	5	17.9±	1.5	0.21±	0.02**	147±	1	3.2±	0.2	104±	1	10.4±	0.3	8.7±	0.5
25 mg/m3	5	17.7±	1.7	0.22±	0.01**	147±	1	3.3±	0.2	104±	1	10.2±	0.2	9.1±	0.8**

Significant difference : * : P ≤ 0.05

** : P ≤ 0.01

Test of Dunnett

TABLE G2

BIOCHEMISTRY : FEMALE

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 MEASURE. TIME : 1
 SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (3W)

Group Name	NO. of Animals	TOTAL PROTEIN g/dl		ALBUMIN g/dl		A/G RATIO		T-BILIRUBIN mg/dl		GLUCOSE mg/dl		T-CHOLESTEROL mg/dl		TRIGLYCERIDE mg/dl	
Control	5	5.4±	0.1	3.2±	0.1	1.5±	0.1	0.02±	0.01	137±	13	72±	5	12±	2
0.2 mg/m3	5	5.5±	0.1	3.2±	0.1	1.5±	0.1	0.02±	0.00	125±	17	76±	8	19±	6
1 mg/m3	5	5.4±	0.1	3.2±	0.1	1.4±	0.1	0.02±	0.00	139±	11	72±	5	16±	5
5 mg/m3	5	5.4±	0.3	3.2±	0.1	1.5±	0.0	0.02±	0.01	139±	8	75±	8	17±	10
25 mg/m3	5	5.6±	0.2	3.3±	0.1	1.5±	0.1	0.02±	0.01	135±	14	81±	7	20±	6

Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr|Cr|j[F344/DuCrj]
 MEASURE. TIME : 1
 SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (3W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dl		AST U/L		ALT U/L		LDH U/L		ALP U/L		G-GTP U/L		CK U/L	
Control	5	128±	7	70±	7	32±	2	184±	199	889±	60	0.9±	0.4	262±	117
0.2 mg/m3	5	142±	12	68±	3	31±	1	88±	11	899±	56	0.9±	0.3	214±	7
1 mg/m3	5	134±	9	70±	6	31±	2	101±	49	911±	69	0.9±	0.2	228±	25
5 mg/m3	5	138±	12	70±	2	29±	1	123±	43	884±	57	1.0±	0.3	240±	20
25 mg/m3	5	144±	9	72±	6	30±	2	157±	80	901±	77	1.4±	0.3	281±	71

Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 MEASURE. TIME : 1
 SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (3W)

Group Name	NO. of Animals	UREA NITROGEN mg/dl		CREATININE mg/dl		SODIUM mEq/l		POTASSIUM mEq/l		CHLORIDE mEq/l		CALCIUM mg/dl		INORGANIC PHOSPHORUS mg/dl	
Control	5	20.5±	1.8	0.26±	0.01	145±	1	3.3±	0.8	105±	2	10.1±	0.3	8.2±	1.4
0.2 mg/m3	5	19.5±	1.1	0.25±	0.02	145±	1	2.9±	0.2	105±	1	10.0±	0.4	7.9±	0.5
1 mg/m3	5	20.3±	2.0	0.23±	0.01	147±	1*	3.2±	0.1	107±	0	10.1±	0.2	8.7±	0.4
5 mg/m3	5	21.9±	2.8	0.24±	0.03	148±	3**	3.2±	0.2	109±	3**	10.0±	0.2	8.6±	0.6
25 mg/m3	5	19.4±	1.9	0.25±	0.01	148±	1**	3.2±	0.3	107±	1	9.9±	0.4	8.7±	0.5

Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett

TABLE H1

BALF : CYTOLOGICAL ANALYSIS : MALE

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j [F344/DuCrj]
 MEASURE TIME : 1
 SEX : MALE

BALF: CYTOLOGICAL ANALYSIS (SUMMARY)
 ALL ANIMALS (3W)

REPORT TYPE : A1

PAGE : 1

Group Name	NO. of Animals	TOTAL CELLS		Differential BALF Cells (%)				EOSINO		ALVEOLAR MACROPHAGE		OTHER	
		$10^3 / \mu l$		NEUTRO	LYMPHO								
Control	5	0.35±	0.06	0.2±	0.3	0.0±	0.1	0.0±	0.0	99.7±	0.2	0.0±	0.0
0.2 mg/mg ³	5	0.35±	0.02	0.3±	0.2	0.0±	0.0	0.0±	0.0	99.7±	0.2	0.0±	0.0
1 mg/mg ³	5	0.40±	0.04	0.2±	0.3	0.0±	0.1	0.0±	0.1	99.7±	0.3	0.0±	0.0
5 mg/mg ³	5	0.33±	0.07	0.4±	0.2	0.0±	0.0	0.0±	0.0	99.6±	0.2	0.0±	0.0
25 mg/mg ³	5	0.29±	0.04	0.4±	0.2	0.0±	0.1	0.0±	0.1	99.5±	0.3	0.0±	0.0

Significant difference: * : P ≤0.05 ** : P ≤0.01 Test of Dunnett

TABLE H2

BALF : CYTOLOGICAL ANALYSIS : FEMALE

S TUDY NO. : 0856

ANIMAL : RAT F344/DuCr1Cr1j [F344/DuCrj]

MEASURE. TIME : 1

SEX : FEMALE

REPORT TYPE : A1

BALF: CYTOLOGICAL ANALYSIS (SUMMARY)

ALL ANIMALS (3W)

PAGE : 2

Group Name	NO. of Animals	TOTAL CELLS		Differential BALF Cells (%)				EOSINO		ALVEOLAR MACROPHAGE		OTHER	
		$10^3 / \mu l$		NEUTRO	LYMPHO								
Control	5	0.26±	0.05	0.3±	0.2	0.0±	0.0	0.0±	0.1	99.7±	0.2	0.0±	0.0
0.2 mg/mg ³	5	0.30±	0.07	0.2±	0.3	0.0±	0.0	0.0±	0.0	99.8±	0.3	0.0±	0.0
1 mg/mg ³	5	0.30±	0.07	0.3±	0.3	0.0±	0.0	0.0±	0.0	99.7±	0.3	0.0±	0.0
5 mg/mg ³	5	0.27±	0.04	0.2±	0.2	0.0±	0.0	0.0±	0.0	99.8±	0.2	0.0±	0.0
25 mg/mg ³	5	0.24±	0.02	0.3±	0.3	0.0±	0.1	0.0±	0.0	99.7±	0.3	0.0±	0.0

Significant difference: * : P ≤0.05 ** : P ≤0.01 Test of Dunnett

TABLE I1

BALF : BIOCHEMICAL ANALYSIS : MALE

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 MEASURE. TIME : 1
 SEX : MALE REPORT TYPE : A1

BALF: BIOCHEMICAL ANALYSIS (SUMMARY)
 ALL ANIMALS (3W)

Group Name	NO. of Animals	TOTAL PROTEIN u g / m L		ALBUMIN u g / m L		LDH U / L		ALP U / L		G-GTP U / L	
Control	5	85±	7	27±	2	40±	4	172±	13	1.3±	0.3
0.2 mg/m3	5	85±	7	29±	3	38±	2	162±	8	1.2±	0.2
1 mg/m3	5	86±	7	29±	3	37±	4	166±	4	1.4±	0.3
5 mg/m3	5	86±	11	28±	3	38±	4	163±	18	1.1±	0.2
25 mg/m3	5	95±	9	31±	3	39±	6	170±	17	1.2±	0.2

Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

TABLE I2

BALF : BIOCHEMICAL ANALYSIS : FEMALE

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 MEASURE. TIME : 1
 SEX : FEMALE REPORT TYPE : A1

BALF: BIOCHEMICAL ANALYSIS (SUMMARY)
 ALL ANIMALS (3W)

Group Name	NO. of Animals	TOTAL PROTEIN u g / m L		ALBUMIN u g / m L		LDH U / L		ALP U / L		G-GTP U / L	
Control	5	82±	2	29±	3	42±	1	142±	7	1.3±	0.2
0.2 mg/m3	5	84±	11	30±	5	41±	5	154±	10	1.5±	0.3
1 mg/m3	5	80±	9	28±	2	38±	5	146±	14	1.5±	0.3
5 mg/m3	5	86±	11	30±	3	38±	3	146±	16	1.4±	0.3
25 mg/m3	5	111±	46	38±	18	46±	14	144±	10	1.4±	0.3

Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

TABLE J1

ORGAN WEIGHT, ABSOLUTE : MALE

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 REPORT TYPE : A1
 SEX : MALE
 UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
 SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	Body Weight		THYMUS		LUNG L		KIDNEYS		SPLEEN		LIVER	
Control	5	149±	8	0.265±	0.034	0.231±	0.015	1.187±	0.078	0.356±	0.038	4.552±	0.224
0.2 mg/m3	5	146±	6	0.273±	0.029	0.238±	0.007	1.198±	0.049	0.369±	0.024	4.364±	0.222
1 mg/m3	5	149±	4	0.271±	0.037	0.233±	0.003	1.209±	0.025	0.374±	0.020	4.407±	0.150
5 mg/m3	5	148±	7	0.272±	0.017	0.235±	0.009	1.225±	0.035	0.376±	0.011	4.465±	0.256
25 mg/m3	5	145±	4	0.278±	0.035	0.240±	0.021	1.207±	0.042	0.362±	0.027	4.365±	0.238

Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01

Test of Dunnett

TABLE J2

ORGAN WEIGHT, ABSOLUTE : FEMALE

STUDY NO. : 0856
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	Body Weight		THYMUS		LUNG L		KIDNEYS		SPLEEN		LIVER	
Control	5	107±	3	0.242±	0.016	0.181±	0.010	0.911±	0.026	0.274±	0.019	3.256±	0.142
0.2 mg/m3	5	105±	3	0.242±	0.020	0.190±	0.013	0.925±	0.041	0.266±	0.021	3.194±	0.198
1 mg/m3	5	103±	6	0.224±	0.022	0.190±	0.010	0.937±	0.041	0.272±	0.041	3.204±	0.204
5 mg/m3	5	103±	2	0.224±	0.006	0.181±	0.005	0.888±	0.043	0.257±	0.015	3.093±	0.080
25 mg/m3	5	99±	5	0.219±	0.019	0.184±	0.017	0.879±	0.059	0.257±	0.023	3.128±	0.226

Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01

Test of Dunnett

TABLE K1

ORGAN WEIGHT, RELATIVE : MALE

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 REPORT TYPE : A1
 SEX : MALE
 UNIT : %

ORGAN WEIGHT:RELATIVE (SUMMARY)
 SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	LUNG L	KIDNEYS	SPLEEN	LIVER
Control	5	149± 8	0.177± 0.019	0.155± 0.006	0.795± 0.010	0.238± 0.013	3.052± 0.029
0.2 mg/m3	5	146± 6	0.188± 0.026	0.163± 0.007	0.822± 0.013	0.253± 0.013	2.993± 0.065
1 mg/m3	5	149± 4	0.181± 0.022	0.157± 0.004	0.812± 0.031	0.251± 0.013	2.958± 0.048
5 mg/m3	5	148± 7	0.185± 0.014	0.159± 0.006	0.831± 0.017*	0.255± 0.008	3.024± 0.067
25 mg/m3	5	145± 4	0.192± 0.020	0.166± 0.012	0.835± 0.018*	0.250± 0.014	3.017± 0.089

Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01

Test of Dunnett

TABLE K2

ORGAN WEIGHT, RELATIVE : FEMALE

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 REPORT TYPE : A1
 SEX : FEMALE
 UNIT : %

ORGAN WEIGHT:RELATIVE (SUMMARY)
 SURVIVAL ANIMALS (3W)

PAGE : 2

Group Name	NO. of Animals	Body Weight (g)	THYMUS	LUNG L	KIDNEYS	SPLEEN	LIVER
Control	5	107± 3	0.227± 0.015	0.170± 0.008	0.853± 0.021	0.257± 0.013	3.049± 0.097
0.2 mg/m3	5	105± 3	0.231± 0.015	0.181± 0.008	0.882± 0.018	0.254± 0.014	3.047± 0.143
1 mg/m3	5	103± 6	0.217± 0.011	0.185± 0.009*	0.913± 0.048	0.263± 0.024	3.117± 0.077
5 mg/m3	5	103± 2	0.218± 0.007	0.176± 0.004	0.865± 0.032	0.251± 0.011	3.015± 0.066
25 mg/m3	5	99± 5	0.220± 0.018	0.185± 0.010*	0.884± 0.039	0.258± 0.012	3.144± 0.099

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL042)

BAIS 5

TABLE L1

HISTOPATHOLOGICAL FINDINGS :
NON-NEOPLASTIC LESIONS : MALE

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 REPORT TYPE : A1
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0- 3W)

Organ	Findings	Group Name No. of Animals on Study				Control 5				0.2 mg/m3 5				1 mg/m3 5				5 mg/m3 5			
		Grade	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)			
[Respiratory system]																					
nasal cavit	goblet cell hyperplasia		< 5>				< 5>				< 5>				< 5>						
			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)				
nasopharynx	goblet cell hyperplasia		< 5>				< 5>				< 5>				< 5>						
			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)				
	deposit of particle:lymphoid tissue		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)				
lung	deposit of particle:alveolar space, phagocytosed by alveolar macrophages		< 5>				< 5>				< 5>				< 5>						
			0	0	0	0	5	0	0	0	5	0	0	0	5	0	0	0			
		(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)				
		deposit of particle:alveolar wall		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)			
	deposit of particle:bronchus-associated lymphoid tissue		0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0			
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)				
	deposit of particle:bronchiole		0	0	0	0	5	0	0	0	5	0	0	0	5	0	0	0			
		(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)				
Grade	1+ : Slight	2+ : Moderate	3+ : Marked	4+ : Severe																	
< a >	a : Number of animals examined at the site																				
b	b : Number of animals with lesion																				
(c)	c : b / a * 100																				

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 REPORT TYPE : A1
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0- 3W)

Organ	Findings	Group Name No. of Animals on Study			
		1+ Grade (%)	2+ Grade (%)	3+ Grade (%)	4+ Grade (%)
25 mg/m3 5					
[Respiratory system]					
nasal cavit	goblet cell hyperplasia	< 5>			
		4 (80)	0 (0)	0 (0)	0 (0)
nasopharynx	goblet cell hyperplasia	< 5>			
		4 (80)	0 (0)	0 (0)	0 (0)
	deposit of particle:lymphoid tissue	2 (40)	0 (0)	0 (0)	0 (0)
lung	deposit of particle:alveolar space, phagocytosed by alveo	< 5>			
		5 (100)	0 (0)	0 (0)	0 (0)
	deposit of particle:alveolar wall	5 (100)	0 (0)	0 (0)	0 (0)
	deposit of particle:bronchus-associated lymphoid tissue	5 (100)	0 (0)	0 (0)	0 (0)
deposit of particle:bronchiole	5 (100)	0 (0)	0 (0)	0 (0)	

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 REPORT TYPE : A1
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0- 3W)

Organ	Findings	Control				0.2 mg/m3				1 mg/m3				5 mg/m3			
		No. of Animals on Study				No. of Animals on Study				No. of Animals on Study				No. of Animals on Study			
Grade		1+	2+	3+	4+	1+	2+	3+	4+	1+	2+	3+	4+	1+	2+	3+	4+
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																	
Lymph node	deposit of particle:mediastinum	< 5>				< 5>				< 5>				< 5>			
		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)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 REPORT TYPE : A1
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0- 3W)

Organ	Findings	Group Name			
		25 mg/m3			
		No. of Animals on Study			
		1+	2+	3+	4+
		(%)	(%)	(%)	(%)

{Hematopoietic system}

Lymph node	deposit of particle:mediastinum	< 5>			
		5	0	0	0
		(100)	(0)	(0)	(0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100

TABLE L2

HISTOPATHOLOGICAL FINDINGS :

NON-NEOPLASTIC LESIONS : FEMALE

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 REPORT TYPE : A1
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0- 3W)

Organ	Findings	Group Name No. of Animals on Study				Control 5				0.2 mg/m3 5				1 mg/m3 5				5 mg/m3 5			
		Grade	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)			
[Respiratory system]																					
nasal cavit	goblet cell hyperplasia		< 5>				< 5>				< 5>				< 5>						
			0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
nasopharynx	goblet cell hyperplasia		< 5>				< 5>				< 5>				< 5>						
			0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
	deposit of particle:lymphoid tissue		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
lung	deposit of particle:alveolar space, phagocytosed by alveolar macrophages		< 5>				< 5>				< 5>				< 5>						
			0	0	0	0	5	0	0	0	5	0	0	0	5	0	0	0			
	deposit of particle:alveolar wall		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
	deposit of particle:bronchus-associated lymphoid tissue		0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0			
deposit of particle:bronchiole		0	0	0	0	5	0	0	0	5	0	0	0	5	0	0	0				

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 REPORT TYPE : A1
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0- 3W)

Organ	Findings	Group Name No. of Animals on Study			
		1+ Grade (%)	2+ Grade (%)	3+ Grade (%)	4+ Grade (%)
25 mg/m3					
5					
[Respiratory system]					
nasal cavit	goblet cell hyperplasia	< 5>			
		2 (40)	0 (0)	0 (0)	0 (0)
nasopharynx	goblet cell hyperplasia	< 5>			
		4 (80)	0 (0)	0 (0)	0 (0)
	deposit of particle:lymphoid tissue	4 (80)	0 (0)	0 (0)	0 (0)
lung	deposit of particle:alveolar space, phagocytosed by alveo	< 5>			
		5 (100)	0 (0)	0 (0)	0 (0)
	deposit of particle:alveolar wall	5 (100)	0 (0)	0 (0)	0 (0)
	deposit of particle:bronchus-associated lymphoid tissue	5 (100)	0 (0)	0 (0)	0 (0)
deposit of particle:bronchiole	5 (100)	0 (0)	0 (0)	0 (0)	

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 REPORT TYPE : A1
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0- 3W)

Organ	Findings	Control				0.2 mg/m3				1 mg/m3				5 mg/m3			
		No. of Animals on Study				No. of Animals on Study				No. of Animals on Study				No. of Animals on Study			
Grade		1+	2+	3+	4+	1+	2+	3+	4+	1+	2+	3+	4+	1+	2+	3+	4+
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																	
Lymph node	deposit of particle:mediastinum	< 5>				< 5>				< 5>				< 5>			
		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)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100

STUDY NO. : 0856
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
 REPORT TYPE : A1
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0- 3W)

Organ	Findings	Group Name			
		25 mg/m3			
		No. of Animals on Study			
		5			
		1+	2+	3+	4+
		(%)	(%)	(%)	(%)

{Hematopoietic system}

Lymph node	deposit of particle:mediastinum	< 5>			
		3	0	0	0
		(60)	(0)	(0)	(0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100

TABLE M

AMOUNT OF TITANIUM DIOXIDE IN THE LUNGS

AMOUNT OF TITANIUM DIOXIDE IN THE LUNGS

Group Name (mg/m ³)		No. of Animals	Amount of Titanium Dioxide	
			µg in 1g Lung	
Male	0	5	0 ±	0
	0.2	5	18.24 ±	2.30
	1	5	63.33 ±	7.55
	5	5	212.92 ±	33.62
	25	5	816.71 ±	156.39
Female	0	5	0 ±	0
	0.2	5	17.04 ±	2.24
	1	5	67.79 ±	6.89
	5	5	221.30 ±	19.96
	25	5	937.11 ±	157.89