

Table 1 Mortality - Female rats

Dose (mg/kg)	Step	Time after administration										Final mortality
		0.5	4 hrs	1	2	3	4	5	6	7	8-14 days	
2000	1st	0	0	0	0	0	0	0	0	0	0	0 / 3 ^a
2000	2nd	0	0	0	0	0	0	0	0	0	0	0 / 3

^a: Cumulative number of animals found dead during the observation period per number of animals treated.

Table 2 Clinical observation - Incidence of signs in female rats

Clinical sign	Dose (mg/kg)	2000		2000	
	Step	1st		2nd	
	Fate	fd	tk	fd	tk
	No. of animals examined	-	3	-	3
No abnormalities detected		-	3	-	3

Fate: fd, found dead; tk, terminal kill.

Table 3 Body weight - Individual values in female rats

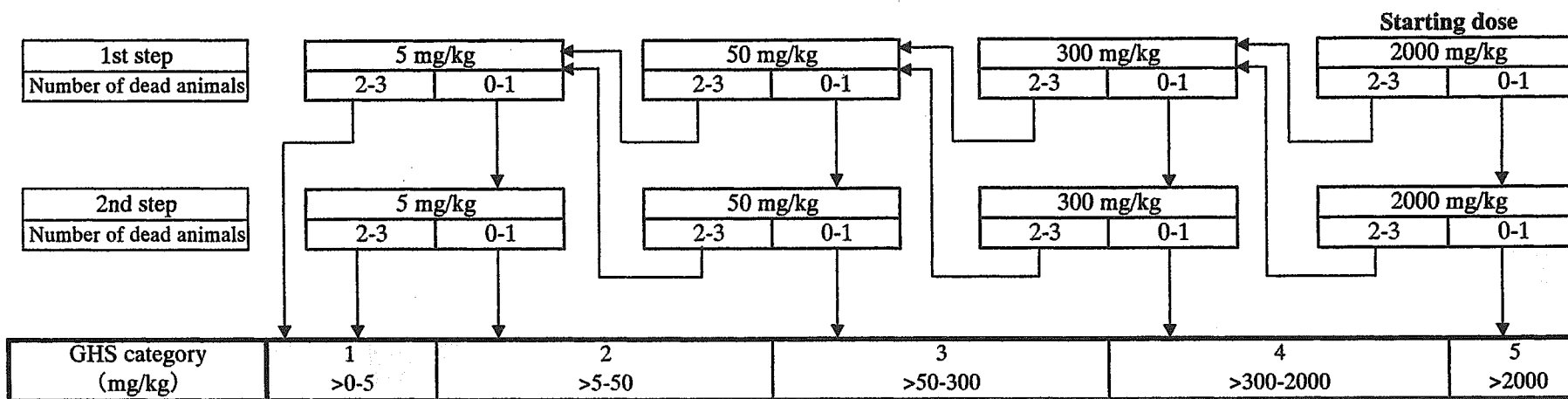
Dose (mg/kg)	Step	Animal number	Before administration	Days after administration	
				7	14
2000	1st	101	140	174	189
		102	142	173	186
		103	153	184	194
2000	2nd	104	147	180	189
		105	151	181	197
		106	143	164	181

Table 4 Necropsy - Incidence of macroscopic lesions in female rats

Site and lesion	Dose (mg/kg)		2000		2000	
	Step		1st		2nd	
	Fate		fd	tk	fd	tk
	No. of animals examined		-	3	-	3
No abnormalities detected		-	3	-	3	

Fate: fd, found dead; tk, terminal kill.

Appendix 1 Flow chart of acute toxic class method with a starting dose of 2000 mg/kg body weight



Appendix 2 Mortality - Identification of scheduled or unscheduled death in female rats

Dose (mg/kg)	Step	Time after administration										
		0.5	4 hrs	1	2	3	4	5	6	7	8-13	14 days
2000	1st											(101) (102)
												(103)
2000	2nd											(104) (105)
												(106)

(n): Scheduled death.

Appendix 3 Clinical observation - Individual data in female rats

Dose (mg/kg)	Step	Animal number	Fate	Time of death	Clinical signs
2000	1st	101	tk	14d	No abnormalities detected
		102	tk	14d	No abnormalities detected
		103	tk	14d	No abnormalities detected
2000	2nd	104	tk	14d	No abnormalities detected
		105	tk	14d	No abnormalities detected
		106	tk	14d	No abnormalities detected

Fate: tk, terminal kill.
Time: d, days.

Appendix 4 Necropsy - Individual macroscopic lesions in female rats

Dose (mg/kg)	Step	Animal number	Fate	Time of death	Macroscopic lesions
2000	1st	101	tk	14d	No abnormalities detected
		102	tk	14d	No abnormalities detected
		103	tk	14d	No abnormalities detected
2000	2nd	104	tk	14d	No abnormalities detected
		105	tk	14d	No abnormalities detected
		106	tk	14d	No abnormalities detected

Fate: tk, terminal kill.

Time: d, days.

Appendix 5

Environmental control - Temperature in the animal room
(Animal Room 116)

(°C)

Day	Month	November	December
Year	2003	2003	
1		-	21.5 ~ 22.1
2		-	21.8 ~ 22.0
3		-	21.9 ~ 22.0
4		-	21.8 ~ 22.0
5		-	21.9 ~ 22.0
6		-	21.9 ~ 21.9
7		-	21.6 ~ 22.0
8		-	21.8 ~ 22.0
9		-	21.8 ~ 22.0
10		-	21.8 ~ 22.2
11		-	21.8 ~ 21.9
12		-	21.8 ~ 22.0
13		-	21.8 ~ 22.0
14		-	21.8 ~ 22.2
15		-	21.8 ~ 22.2
16		-	21.8 ~ 22.0
17		-	-
18		21.8 ~ 22.0	-
19		21.8 ~ 22.0	-
20		21.8 ~ 22.0	-
21		21.9 ~ 22.0	-
22		21.9 ~ 22.2	-
23		21.9 ~ 22.1	-
24		21.8 ~ 22.0	-
25		21.8 ~ 21.9	-
26		21.8 ~ 22.0	-
27		21.8 ~ 22.0	-
28		21.8 ~ 22.0	-
29		21.9 ~ 22.0	-
30		21.8 ~ 22.0	-
31		-	-

-: Data not shown because of the absence of animals in the room.

Appendix 6 Environmental control - Humidity in the animal room
(Animal Room 116)

		(%)	
Month	November	December	
Day	Year	2003	2003
1		-	47.8 ~ 59.1
2		-	52.8 ~ 71.3 ^a
3		-	51.7 ~ 55.1
4		-	52.2 ~ 55.9
5		-	52.7 ~ 58.3
6		-	55.3 ~ 59.4
7		-	53.1 ~ 60.8
8		-	53.0 ~ 61.1
9		-	53.0 ~ 64.5
10		-	52.6 ~ 61.5
11		-	50.8 ~ 57.6
12		-	55.4 ~ 60.2
13		-	54.7 ~ 64.8
14		-	53.5 ~ 61.4
15		-	52.9 ~ 62.7
16		-	53.2 ~ 64.4
17		-	-
18		50.1 ~ 54.2	-
19		50.3 ~ 52.5	-
20		49.8 ~ 51.6	-
21		47.6 ~ 54.0	-
22		47.2 ~ 58.7	-
23		49.5 ~ 54.9	-
24		49.9 ~ 53.5	-
25		49.4 ~ 56.1	-
26		49.0 ~ 55.2	-
27		53.0 ~ 56.4	-
28		53.3 ~ 59.8	-
29		53.2 ~ 57.1	-
30		48.2 ~ 58.2	-
31		-	-

-: Data not shown because of the absence of animals in the room.

a: A temporal rise following cleaning of the animal room (≤ 1.8 h).