

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 3 Body weight (males)

Body weight (kg)

Sex: Male		Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Day(s) Relative to Start Date							
1	Mean	3.24 ¹	3.14	3.22	3.16	3.03	3.11
	S.D.	0.30	0.33	0.42	0.44	0.35	0.52
	N	4	4	4	4	4	4
4	Mean	3.26 ¹	3.17	3.29	3.20	3.06	3.04
	S.D.	0.32	0.34	0.40	0.45	0.32	0.47
	N	4	4	4	4	4	4
8	Mean	3.25 ¹	3.16	3.28	3.22	3.07	3.05
	S.D.	0.33	0.37	0.42	0.47	0.37	0.51
	N	4	4	4	4	4	4
11 or 12	Mean	3.31 ¹	3.19	3.32	3.31	3.13	3.01
	S.D.	0.33	0.37	0.44	0.49	0.40	0.46
	N	4	4	4	4	4	4
15	Mean	3.30 ¹	3.19	3.26	3.25	3.07	2.89
	S.D.	0.34	0.36	0.43	0.45	0.40	0.37
	N	4	4	4	4	4	4
18	Mean	3.35 ¹	3.19	3.26	3.21	3.12	2.84
	S.D.	0.34	0.35	0.43	0.47	0.42	0.33
	N	4	4	4	4	4	3

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [1 - Automatic Transformation Selected: Identity (No Transformation)]

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 3 Body weight (males)

Body weight (kg)

Sex: Male		Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Day(s) Relative to Start Date							
22	Mean	3.38 ¹	3.20	3.28	3.27	3.11	2.82
	S.D.	0.32	0.39	0.41	0.48	0.44	0.36
	N	4	4	4	4	4	3
25	Mean	3.37 ¹	3.21	3.29	3.28	3.11	2.82
	S.D.	0.34	0.38	0.46	0.48	0.43	0.36
	N	4	4	4	4	4	3
28	Mean	3.42 ¹	3.22	3.44	3.31	3.19	2.88
	S.D.	0.31	0.38	0.43	0.49	0.41	0.33
	N	4	4	4	4	4	3

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [1 - Automatic Transformation Selected: Identity (No Transformation)]

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 4 Body weight (females)

Body weight (kg)

Sex: Female		Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Day(s) Relative to Start Date							
1	Mean	2.73 ¹	2.72	2.76	2.66	2.71	2.69
	S.D.	0.35	0.31	0.26	0.33	0.38	0.26
	N	4	4	4	4	4	4
4	Mean	2.74 ¹	2.73	2.75	2.62	2.68	2.65
	S.D.	0.39	0.29	0.25	0.32	0.34	0.29
	N	4	4	4	4	4	4
8	Mean	2.78 ¹	2.77	2.72	2.62	2.69	2.55
	S.D.	0.35	0.32	0.22	0.30	0.31	0.29
	N	4	4	4	4	4	4
11	Mean	2.82 ¹	2.80	2.74	2.70	2.70	2.55
	S.D.	0.39	0.33	0.25	0.29	0.33	0.29
	N	4	4	4	4	4	4
15	Mean	2.82 ¹	2.80	2.72	2.64	2.63	2.49
	S.D.	0.39	0.30	0.28	0.28	0.35	0.31
	N	4	4	4	4	4	4
18	Mean	2.83 ¹	2.82	2.70	2.66	2.68	2.41
	S.D.	0.43	0.35	0.27	0.30	0.33	0.33
	N	4	4	4	4	4	4

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [I - Automatic Transformation Selected: Identity (No Transformation)]

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 4 Body weight (females)

Body weight (kg)

Sex: Female		Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Day(s) Relative to Start Date							
22	Mean	2.84 ¹	2.85	2.74	2.68	2.72	2.65 ^{n1²}
	S.D.	0.39	0.37	0.28	0.28	0.36	.
	N	4	4	4	4	4	1
25	Mean	2.87 ¹	2.85	2.78	2.79	2.78	2.73 ^{n1²}
	S.D.	0.43	0.40	0.26	0.39	0.35	.
	N	4	4	4	4	4	1
28	Mean	2.91 ¹	2.87	2.80	2.79	2.86	2.69 ^{n1²}
	S.D.	0.39	0.41	0.28	0.37	0.37	.
	N	4	4	4	4	4	1

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [1 - Automatic Transformation Selected: Identity (No Transformation)]

2 [n1 - This group has only one value: Data was not statistically analyzed.]

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 5 Food consumption (males)

Sex: Male		Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Day(s) Relative to Start Date							
-4	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
-3	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
-2	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
-1	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
1	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
2	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
3	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4

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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 5 Food consumption (males)

Sex: Male		Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Day(s) Relative to Start Date							
4	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
5	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
6	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
7	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
8	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
9	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
10	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 5 Food consumption (males)

Sex: Male		Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Day(s) Relative to Start Date							
11	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
12	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
13	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	4
14	Mean	100 ¹	100	100	100	100	95
	S.D.	0	0	0	0	0	10
	N	4	4	4	4	4	4
15	Mean	100 ¹	100	100	100	100	75
	S.D.	0	0	0	0	0	50
	N	4	4	4	4	4	4
16	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	3
17	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	3

Statistical Test: Generalised Anova/Ancova Test Transformation: Automatic

1 [1 - Automatic Transformation Selected: Identity (No Transformation)]

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A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 5 Food consumption (males)

Sex: Male		Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Day(s) Relative to Start Date							
18	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	3
19	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	3
20	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	3
21	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	3
22	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	3
23	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	3
24	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	3

A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

Table 5 Food consumption (males)

Sex: Male		Control 0.5%CMC-Na	Low TM5509 2 mg/kg/day	Low-Mid TM5509 6 mg/kg/day	Mid TM5509 20 mg/kg/day	Mid-High TM5509 80 mg/kg/day	High TM5509 300 mg/kg/day
Day(s) Relative to Start Date							
25	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	3
26	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	3
27	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	3
28	Mean	100	100	100	100	100	100
	S.D.	0	0	0	0	0	0
	N	4	4	4	4	4	3