

TK13152

Page: 1

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

Table 24 Plasma concentrations and toxicokinetic parameters of TM5509 (females)

Sex: Female Day: 1

Group	Animal No.	Plasma concentration ($\mu\text{g/mL}$)					C_{max} ($\mu\text{g/mL}$)	T_{max} (h)	$\text{AUC}_{0-24\text{h}}$ ^{a)} ($\mu\text{g}\cdot\text{h/mL}$)
		Time post-dosing							
		1h	4h	6h	8h	24h			
Control 0.5%CMC-Na	RP1F01	BLQ [1]	BLQ [1]	BLQ [1]	BLQ [1]	BLQ [1]	-	-	-
	RP1F02	BLQ [1]	BLQ [1]	BLQ [1]	BLQ [1]	BLQ [1]	-	-	-
	RP1F03	BLQ [1]	BLQ [1]	BLQ [1]	BLQ [1]	BLQ [1]	-	-	-
	RP1F04	BLQ [1]	BLQ [1]	BLQ [1]	BLQ [1]	BLQ [1]	-	-	-
	Mean	NC	NC	NC	NC	NC	-	-	-
	S.D.	NC	NC	NC	NC	NC	-	-	-
	N	4	4	4	4	4	-	-	-
Low TM5509 2 mg/kg/day	RP2F01	23.1 [1]	27.2 [1]	26.2 [1]	20.2 [1]	7.12 [1]	27.2	4	405
	RP2F02	11.1 [1]	32.4 [1]	29.0 [1]	25.0 [1]	8.83 [1]	32.4	4	457
	RP2F03	23.8 [1]	27.3 [1]	28.8 [1]	23.5 [1]	7.21 [1]	28.8	6	443
	RP2F04	22.6 [1]	30.1 [1]	27.0 [1]	21.5 [1]	9.25 [1]	30.1	4	442
	Mean	20.2	29.3	27.8	22.6	8.10	29.6	4.5	437
	S.D.	6.1	2.5	1.4	2.1	1.10	2.2	1.0	22
	N	4	4	4	4	4	4	4	4
Low-Mid TM5509 6 mg/kg/day	RP3F01	46.8 [3]	85.8 [3]	74.1 [3]	60.7 [3]	14.4 [1]	85.8	4	1120
	RP3F02	25.1 [3]	80.7 [3]	73.9 [3]	58.2 [3]	10.6 [1]	80.7	4	1010
	RP3F03	20.8 [3]	82.3 [3]	76.5 [3]	65.8 [3]	21.9 [1]	82.3	4	1170
	RP3F04	72.8 [3]	77.7 [3]	69.3 [3]	54.4 [3]	9.93 [1]	77.7	4	1050
	Mean	41.4	81.6	73.5	59.8	14.2	81.6	4.0	1090
	S.D.	23.8	3.4	3.0	4.8	5.5	3.4	0.0	70
	N	4	4	4	4	4	4	4	4

General Footnote: []: Dilution factor

BLQ: Below the lower limit of quantification (0.5 $\mu\text{g/mL}$)

NC: Not calculated

^{a)} The values of 0 hours were regarded as 0 $\mu\text{g/mL}$.

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

Table 24 Plasma concentrations and toxicokinetic parameters of TM5509 (females)

Sex: Female Day: 1

Group	Animal No.	Plasma concentration ($\mu\text{g/mL}$)					C_{max} ($\mu\text{g/mL}$)	T_{max} (h)	$\text{AUC}_{0-24\text{h}}$ ^{a)} ($\mu\text{g}\cdot\text{h/mL}$)
		Time post-dosing							
		1h	4h	6h	8h	24h			
Mid TM5509 20 mg/kg/day	RP4F01	57.0 [6]	181 [6]	179 [6]	174 [6]	35.5 [3]	181	4	2770
	RP4F02	101 [6]	130 [6]	129 [6]	133 [6]	53.3 [3]	133	8	2410
	RP4F03	92.9 [6]	174 [6]	144 [6]	138 [6]	33.1 [3]	174	4	2420
	RP4F04	66.4 [6]	154 [6]	156 [6]	142 [6]	38.7 [3]	156	6	2420
	Mean	79.3	160	152	147	40.2	161	5.5	2510
	S.D.	21.0	23	21	19	9.1	21	1.9	180
	N	4	4	4	4	4	4	4	4
Mid-High TM5509 80 mg/kg/day	RP5F01	91.4 [6]	194 [6]	207 [6]	194 [6]	50.8 [3]	207	6	3230
	RP5F02	155 [6]	162 [6]	202 [6]	213 [6]	81.8 [3]	213	8	3690
	RP5F03	129 [6]	191 [6]	191 [6]	202 [6]	38.0 [3]	202	8	3240
	RP5F04	119 [6]	193 [6]	203 [6]	203 [6]	58.3 [3]	203	6	3420
	Mean	124	185	201	203	57.2	206	7.0	3400
	S.D.	26	15	7	8	18.4	5	1.2	220
	N	4	4	4	4	4	4	4	4
High TM5509 300 mg/kg/day	RP6F01	161 [6]	225 [6]	217 [6]	229 [6]	63.1 [6]	229	8	3880
	RP6F02	117 [6]	227 [6]	252 [6]	274 [6]	144 [6]	274	8	4920
	RP6F03	180 [6]	239 [6]	263 [6]	297 [6]	160 [6]	297	8	5440
	RP6F04	123 [6]	204 [6]	202 [6]	212 [6]	76.1 [6]	212	8	3680
	Mean	145	224	234	253	111	253	8.0	4480
	S.D.	30	15	29	39	48	39	0.0	840
	N	4	4	4	4	4	4	4	4

General Footnote: []: Dilution factor

^{a)} The values of 0 hours were regarded as 0 $\mu\text{g/mL}$.

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

Table 24 Plasma concentrations and toxicokinetic parameters of TM5509 (females)

Sex: Female Day: 28

Group	Animal No.	Plasma concentration (µg/mL)						C _{max} (µg/mL)	T _{max} (h)	AUC _{0-24h} ^{a)} (µg·h/mL)
		Pre-dosing	Time post-dosing							
			1h	4h	6h	8h	24h			
Control 0.5%CMC-Na	RP1F01	BLQ [1]	BLQ [1]	BLQ [1]	BLQ [1]	BLQ [1]	BLQ [1]	-	-	-
	RP1F02	BLQ [1]	BLQ [1]	BLQ [1]	BLQ [1]	BLQ [1]	BLQ [1]	-	-	-
	RP1F03	BLQ [1]	BLQ [1]	BLQ [1]	BLQ [1]	BLQ [1]	BLQ [1]	-	-	-
	RP1F04	BLQ [1]	BLQ [1]	BLQ [1]	BLQ [1]	BLQ [1]	BLQ [1]	-	-	-
	Mean	NC	NC	NC	NC	NC	NC	-	-	-
	S.D.	NC	NC	NC	NC	NC	NC	-	-	-
	N	4	4	4	4	4	4	-	-	-
Low TM5509 2 mg/kg/day	RP2F01	12.5 [1]	34.4 [1]	35.9 [1]	35.2 [1]	30.2 [1]	8.67 [1]	35.9	4	576
	RP2F02	14.3 [1]	29.9 [1]	40.5 [1]	41.4 [1]	34.5 [1]	16.8 [1]	41.4	6	696
	RP2F03	12.9 [1]	29.8 [1]	40.1 [1]	33.4 [1]	30.1 [1]	11.2 [1]	40.1	4	594
	RP2F04	9.89 [1]	28.7 [1]	33.1 [1]	28.6 [1]	21.3 [1]	11.0 [1]	33.1	4	482
	Mean	12.4	30.7	37.4	34.7	29.0	11.9	37.6	4.5	587
	S.D.	1.8	2.5	3.5	5.3	5.5	3.5	3.8	1.0	88
	N	4	4	4	4	4	4	4	4	4
Low-Mid TM5509 6 mg/kg/day	RP3F01	9.76 [1]	75.1 [3]	78.8 [3]	64.1 [3]	50.1 [3]	9.77 [1]	78.8	4	1010
	RP3F02	13.5 [1]	44.2 [3]	91.1 [3]	78.8 [3]	67.9 [3]	11.1 [1]	91.1	4	1180
	RP3F03	23.3 [1]	49.3 [3]	73.0 [3]	79.0 [3]	66.3 [3]	20.6 [1]	79.0	6	1210
	RP3F04	9.47 [1]	61.7 [3]	59.6 [3]	48.4 [3]	34.1 [3]	9.11 [1]	61.7	1	754
	Mean	14.0	57.6	75.6	67.6	54.6	12.6	77.7	3.8	1040
	S.D.	6.5	13.8	13.1	14.6	15.9	5.4	12.1	2.1	210
	N	4	4	4	4	4	4	4	4	4

General Footnote: []: Dilution factor

BLQ: Below the lower limit of quantification (0.5 µg/mL)

NC: Not calculated

^{a)} The values of 0 hours were calculated using the pretreatment value.

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

Table 24 Plasma concentrations and toxicokinetic parameters of TM5509 (females)

Sex: Female Day: 28

Group	Animal No.	Plasma concentration (µg/mL)						C _{max} (µg/mL)	T _{max} (h)	AUC _{0-24h} ^{a)} (µg·h/mL)
		Pre-dosing	Time post-dosing							
			1h	4h	6h	8h	24h			
Mid TM5509 20 mg/kg/day	RP4F01	33.4 [3]	52.9 [6]	148 [6]	124 [6]	115 [6]	30.9 [3]	148	4	2020
	RP4F02	40.3 [3]	86.3 [6]	126 [6]	124 [6]	123 [6]	32.3 [3]	126	4	2120
	RP4F03	27.0 [3]	96.1 [6]	113 [6]	112 [6]	106 [6]	25.8 [3]	113	4	1870
	RP4F04	13.2 [3]	69.0 [6]	84.2 [6]	75.9 [6]	69.9 [6]	14.0 [3]	84.2	4	1250
	Mean	28.5	76.1	118	109	103	25.8	118	4.0	1820
	S.D.	11.5	19.1	27	23	23	8.3	27	0.0	390
	N	4	4	4	4	4	4	4	4	4
Mid-High TM5509 80 mg/kg/day	RP5F01	28.3 [3]	91.8 [6]	150 [6]	127 [6]	150 [6]	29.8 [3]	150	4	2420
	RP5F02	34.7 [3]	63.2 [6]	133 [6]	109 [6]	98.8 [6]	27.4 [3]	133	4	1800
	RP5F03	39.3 [3]	70.0 [6]	117 [6]	101 [6]	122 [6]	39.6 [3]	122	8	2070
	RP5F04	56.5 [3]	131 [6]	147 [6]	170 [6]	187 [6]	43.0 [3]	187	8	3020
	Mean	39.7	89.0	137	127	139	35.0	148	6.0	2330
	S.D.	12.1	30.5	15	31	38	7.5	28	2.3	530
	N	4	4	4	4	4	4	4	4	4
High TM5509 300 mg/kg/day	RP6F01 ^{b)}	-	-	-	-	-	-	-	-	-
	RP6F02	64.9 [6]	123 [6]	123 [6]	118 [10]	150 [10]	57.5 [6]	150	8	2630
	RP6F03 ^{c)}	-	-	-	-	-	-	-	-	-
	RP6F04 ^{c)}	-	-	-	-	-	-	-	-	-
	Mean	NC	NC	NC	NC	NC	NC	NC	NC	NC
	S.D.	NC	NC	NC	NC	NC	NC	NC	NC	NC
	N	1	1	1	1	1	1	1	1	1

General Footnote: []: Dilution factor

NC: Not calculated

^{a)} The values of 0 hours were calculated using the pretreatment value.^{b)} Died on Day 20 of dosing^{c)} Necropsied on Day 19 of dosing due to a moribund condition

TK13152

Page: 2

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

Appendix 1 Body weight (males)

Sex: Male Body weight (kg)

Low TM5509 2 mg/kg/day	Day(s) Relative to Start Date										
	-5	-4	1	4	8	11 or 12	15	18	22	25	28
RP2M01	.	3.54	3.56	3.57	3.63	3.63	3.61	3.61	3.65	3.64	3.65
RP2M02	.	2.88	2.91	2.87	2.87	2.89	2.92	2.92	2.91	2.97	2.90
RP2M03	3.16	.	3.23	3.33	3.26	3.37	3.35	3.35	3.39	3.39	3.42
RP2M04	2.71	.	2.85	2.90	2.86	2.87	2.86	2.88	2.83	2.82	2.91
Mean	2.94	3.21	3.14	3.17	3.16	3.19	3.19	3.19	3.20	3.21	3.22
S.D.	0.32	0.47	0.33	0.34	0.37	0.37	0.36	0.35	0.39	0.38	0.38
N	2	2	4	4	4	4	4	4	4	4	4

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

Appendix 1 Body weight (males)

Sex: Male Body weight (kg)

Low-Mid TM5509 6 mg/kg/day	Day(s) Relative to Start Date										
	-5	-4	1	4	8	11 or 12	15	18	22	25	28
RP3M01	.	2.73	2.82	2.91	2.86	2.91	2.89	2.86	2.89	2.82	3.02
RP3M02	.	3.03	2.97	3.06	3.07	3.02	2.95	3.01	3.06	3.08	3.29
RP3M03	3.72	.	3.76	3.82	3.82	3.88	3.82	3.84	3.83	3.90	4.04
RP3M04	3.27	.	3.33	3.36	3.36	3.46	3.36	3.31	3.32	3.34	3.39
Mean	3.50	2.88	3.22	3.29	3.28	3.32	3.26	3.26	3.28	3.29	3.44
S.D.	0.32	0.21	0.42	0.40	0.42	0.44	0.43	0.43	0.41	0.46	0.43
N	2	2	4	4	4	4	4	4	4	4	4

TK13152

Page: 4

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

Appendix 1 Body weight (males)

Sex: Male Body weight (kg)

Mid TM5509 20 mg/kg/day	Day(s) Relative to Start Date										
	-5	-4	1	4	8	11 or 12	15	18	22	25	28
RP4M01	.	3.74	3.74	3.79	3.83	3.92	3.83	3.83	3.90	3.92	4.00
RP4M02	.	2.58	2.66	2.69	2.70	2.73	2.72	2.69	2.74	2.76	2.85
RP4M03	2.93	.	3.11	3.16	3.14	3.28	3.19	3.13	3.17	3.16	3.16
RP4M04	3.14	.	3.13	3.15	3.21	3.29	3.25	3.20	3.28	3.29	3.23
Mean	3.04	3.16	3.16	3.20	3.22	3.31	3.25	3.21	3.27	3.28	3.31
S.D.	0.15	0.82	0.44	0.45	0.47	0.49	0.45	0.47	0.48	0.48	0.49
N	2	2	4	4	4	4	4	4	4	4	4

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

Appendix 1 Body weight (males)

Sex: Male Body weight (kg)

Mid-High TM5509 80 mg/kg/day	Day(s) Relative to Start Date										
	-5	-4	1	4	8	11 or 12	15	18	22	25	28
RP5M01	.	3.06	2.98	3.09	3.06	3.16	3.10	3.09	3.10	3.06	3.16
RP5M02	.	2.53	2.58	2.65	2.60	2.60	2.55	2.60	2.57	2.59	2.68
RP5M03	3.18	.	3.11	3.07	3.12	3.19	3.11	3.16	3.14	3.14	3.24
RP5M04	3.35	.	3.43	3.42	3.49	3.57	3.52	3.63	3.64	3.65	3.67
Mean	3.27	2.80	3.03	3.06	3.07	3.13	3.07	3.12	3.11	3.11	3.19
S.D.	0.12	0.37	0.35	0.32	0.37	0.40	0.40	0.42	0.44	0.43	0.41
N	2	2	4	4	4	4	4	4	4	4	4

TK13152

Page: 6

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

Appendix 1 Body weight (males)

Sex: Male Body weight (kg)

High TM5509 300 mg/kg/day	Day(s) Relative to Start Date										
	-5	-4	1	4	8	11 or 12	15	18	22	25	28
RP6M01	.	2.49	2.44	2.45	2.40	2.47	2.39	2.47	2.42	2.42	2.51
RP6M02	.	3.57	3.67	3.59	3.65	3.58	3.28
RP6M03	3.23	.	3.28	3.16	3.13	3.07	2.96	3.10	3.12	3.12	3.14
RP6M04	2.93	.	3.03	2.94	3.03	2.93	2.91	2.95	2.92	2.91	2.99
Mean	3.08	3.03	3.11	3.04	3.05	3.01	2.89	2.84	2.82	2.82	2.88
S.D.	0.21	0.76	0.52	0.47	0.51	0.46	0.37	0.33	0.36	0.36	0.33
N	2	2	4	4	4	4	4	3	3	3	3

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

Appendix 2 Body weight (females)

Sex: Female Body weight (kg)

Control 0.5%CMC-Na	Day(s) Relative to Start Date										
	-5	-4	1	4	8	11	15	18	22	25	28
RP1F01	.	2.60	2.54	2.56	2.61	2.68	2.66	2.63	2.65	2.71	2.74
RP1F02	.	3.12	3.20	3.28	3.26	3.35	3.38	3.44	3.41	3.50	3.47
RP1F03	2.32	.	2.39	2.38	2.45	2.44	2.47	2.47	2.54	2.52	2.59
RP1F04	2.70	.	2.77	2.74	2.81	2.81	2.77	2.78	2.74	2.76	2.82
Mean	2.51	2.86	2.73	2.74	2.78	2.82	2.82	2.83	2.84	2.87	2.91
S.D.	0.27	0.37	0.35	0.39	0.35	0.39	0.39	0.43	0.39	0.43	0.39
N	2	2	4	4	4	4	4	4	4	4	4

TK13152

Page: 2

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

Appendix 2 Body weight (females)

Sex: Female Body weight (kg)

Low TM5509 2 mg/kg/day	Day(s) Relative to Start Date										
	-5	-4	1	4	8	11	15	18	22	25	28
RP2F01	.	2.40	2.37	2.40	2.39	2.38	2.47	2.43	2.41	2.36	2.38
RP2F02	.	2.67	2.63	2.68	2.72	2.80	2.72	2.74	2.80	2.80	2.77
RP2F03	3.23	.	3.12	3.11	3.18	3.20	3.20	3.27	3.30	3.33	3.36
RP2F04	2.80	.	2.75	2.72	2.79	2.81	2.80	2.83	2.89	2.91	2.96
Mean	3.02	2.54	2.72	2.73	2.77	2.80	2.80	2.82	2.85	2.85	2.87
S.D.	0.30	0.19	0.31	0.29	0.32	0.33	0.30	0.35	0.37	0.40	0.41
N	2	2	4	4	4	4	4	4	4	4	4

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

Appendix 2 Body weight (females)

Sex: Female Body weight (kg)

Low-Mid TM5509 6 mg/kg/day	Day(s) Relative to Start Date										
	-5	-4	1	4	8	11	15	18	22	25	28
RP3F01	.	2.91	2.99	2.91	2.81	2.85	2.80	2.77	2.85	2.92	2.83
RP3F02	.	2.58	2.59	2.60	2.66	2.76	2.68	2.64	2.66	2.69	2.67
RP3F03	2.56	.	2.48	2.47	2.44	2.39	2.36	2.37	2.39	2.46	2.51
RP3F04	2.98	.	2.96	3.00	2.96	2.96	3.03	3.03	3.05	3.06	3.17
Mean	2.77	2.75	2.76	2.75	2.72	2.74	2.72	2.70	2.74	2.78	2.80
S.D.	0.30	0.23	0.26	0.25	0.22	0.25	0.28	0.27	0.28	0.26	0.28
N	2	2	4	4	4	4	4	4	4	4	4

TK13152

Page: 4

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

Appendix 2 Body weight (females)

Sex: Female Body weight (kg)

Mid TM5509 20 mg/kg/day	Day(s) Relative to Start Date										
	-5	-4	1	4	8	11	15	18	22	25	28
RP4F01	.	2.50	2.52	2.40	2.46	2.60	2.49	2.46	2.50	2.52	2.52
RP4F02	.	2.66	2.69	2.72	2.67	2.76	2.71	2.67	2.74	2.78	2.83
RP4F03	2.28	.	2.32	2.34	2.33	2.37	2.35	2.41	2.43	2.51	2.51
RP4F04	3.15	.	3.10	3.03	3.02	3.05	2.99	3.08	3.06	3.34	3.30
Mean	2.72	2.58	2.66	2.62	2.62	2.70	2.64	2.66	2.68	2.79	2.79
S.D.	0.62	0.11	0.33	0.32	0.30	0.29	0.28	0.30	0.28	0.39	0.37
N	2	2	4	4	4	4	4	4	4	4	4

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

Appendix 2 Body weight (females)

Sex: Female Body weight (kg)

Mid-High TM5509 80 mg/kg/day	Day(s) Relative to Start Date										
	-5	-4	1	4	8	11	15	18	22	25	28
RP5F01	.	3.13	3.23	3.13	3.09	3.12	3.08	3.08	3.17	3.23	3.37
RP5F02	.	2.62	2.56	2.53	2.54	2.60	2.53	2.60	2.66	2.71	2.74
RP5F03	2.66	.	2.73	2.70	2.76	2.76	2.68	2.74	2.75	2.78	2.81
RP5F04	2.34	.	2.33	2.34	2.38	2.32	2.23	2.28	2.29	2.39	2.50
Mean	2.50	2.88	2.71	2.68	2.69	2.70	2.63	2.68	2.72	2.78	2.86
S.D.	0.23	0.36	0.38	0.34	0.31	0.33	0.35	0.33	0.36	0.35	0.37
N	2	2	4	4	4	4	4	4	4	4	4

TK13152

Page: 6

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

Appendix 2 Body weight (females)

Sex: Female Body weight (kg)

High TM5509 300 mg/kg/day	Day(s) Relative to Start Date										
	-5	-4	1	4	8	11	15	18	22	25	28
RP6F01	.	3.03	3.02	2.97	2.87	2.90	2.81	2.73	.	.	.
RP6F02	.	2.72	2.76	2.79	2.67	2.65	2.67	2.63	2.65	2.73	2.69
RP6F03	2.46	.	2.42	2.32	2.20	2.24	2.13	2.06	.	.	.
RP6F04	2.57	.	2.57	2.50	2.45	2.40	2.35	2.20	.	.	.
Mean	2.52	2.88	2.69	2.65	2.55	2.55	2.49	2.41	2.65	2.73	2.69
S.D.	0.08	0.22	0.26	0.29	0.29	0.29	0.31	0.33	.	.	.
N	2	2	4	4	4	4	4	4	1	1	1

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

Appendix 3 Food consumption (males)

Sex: Male Food consumption (g/day)

Control 0.5%CMC-Na	Day(s) Relative to Start Date																		
	-5	-4	-3	-2	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14
RP1M01	.	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
RP1M02	.	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
RP1M03	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
RP1M04	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
Mean	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
S.D.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
N	2	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 2

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

Appendix 3 Food consumption (males)

Sex: Male Food consumption (g/day)

Control 0.5%CMC-Na	Day(s) Relative to Start Date													
	15	16	17	18	19	20	21	22	23	24	25	26	27	28
RP1M01	100	100	100	100	100	100	100	100	100	100	100	100	100	100
RP1M02	100	100	100	100	100	100	100	100	100	100	100	100	100	100
RP1M03	100	100	100	100	100	100	100	100	100	100	100	100	100	100
RP1M04	100	100	100	100	100	100	100	100	100	100	100	100	100	100
Mean	100	100	100	100	100	100	100	100	100	100	100	100	100	100
S.D.	0	0	0	0	0	0	0	0	0	0	0	0	0	0
N	4	4	4	4	4	4	4	4	4	4	4	4	4	4

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

Appendix 3 Food consumption (males)

Sex: Male Food consumption (g/day)

Low TM5509 2 mg/kg/day	Day(s) Relative to Start Date																		
	-5	-4	-3	-2	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14
RP2M01	.	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
RP2M02	.	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
RP2M03	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
RP2M04	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
Mean	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
S.D.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
N	2	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 4

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

Appendix 3 Food consumption (males)

Sex: Male Food consumption (g/day)

Low TM5509 2 mg/kg/day	Day(s) Relative to Start Date													
	15	16	17	18	19	20	21	22	23	24	25	26	27	28
RP2M01	100	100	100	100	100	100	100	100	100	100	100	100	100	100
RP2M02	100	100	100	100	100	100	100	100	100	100	100	100	100	100
RP2M03	100	100	100	100	100	100	100	100	100	100	100	100	100	100
RP2M04	100	100	100	100	100	100	100	100	100	100	100	100	100	100
Mean	100	100	100	100	100	100	100	100	100	100	100	100	100	100
S.D.	0	0	0	0	0	0	0	0	0	0	0	0	0	0
N	4	4	4	4	4	4	4	4	4	4	4	4	4	4

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

Appendix 3 Food consumption (males)

Sex: Male Food consumption (g/day)

Low-Mid TM5509 6 mg/kg/day	Day(s) Relative to Start Date																		
	-5	-4	-3	-2	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14
RP3M01	.	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
RP3M02	.	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
RP3M03	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
RP3M04	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
Mean	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
S.D.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
N	2	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4